

FIG.1



GGC ACC GGG GCG CCG CCG CCG CTG CTG CTA CTG CCG CTG CTG CTG CTC CTA GGG ACC GGC  
Gly Thr Gly Ala Pro Pro Pro Leu Leu Leu Leu Pro Leu Leu Leu Leu Leu Gly Thr Gly

CTC TTG CCT GCT AGC AGC CAC ATA GAG ACC CGG GCC CAT GCG GAG GAG CGG CTC CTG AAG  
Leu Leu Pro Ala Ser Ser His Ile Glu Thr Arg Ala His Ala Glu Glu Arg Leu Leu Lys

AGA CTC TTC TCC GGT TAC AAC AAG TGG TCT CGG CCA GTA GGC AAT ATC TCA GAT GTG GTC  
Arg Leu Phe Ser Gly Tyr Asn Lys Trp Ser Arg Pro Val Gly Asn Ile Ser Asp Val Val

CTC GTC CCG TTT GGC TTG TCC ATT GCT CAG CTC ATT GAC GTG GAC GAG AAG AAC CAG ATG  
Leu Val Arg Phe Gly Leu Ser Ile Ala Gln Leu Ile Asp Val Asp Glu Lys Asn Gln Met

ATG ACA ACC AAC GTG TGG GTG AAG CAG GAG TGG CAC GAC TAC AAG CTG CGC TGG GAC CCT  
Met Thr Thr Asn Val Trp Val Lys Gln Glu Trp His Asp Tyr Lys Leu Arg Trp Asp Pro

GGT GAC TAC GAG AAT GTC ACC TCC ATC CCG ATC CCC TCT GAA CTC ATC TGG AGG CCT GAC  
Gly Asp Tyr Glu Asn Val Thr Ser Ile Arg Ile Pro Ser Glu Leu Ile Trp Arg Pro Asp

ATC GTC CTC TAC AAC AAT GCG GAT GGA GAC TTT GCA GTC ACC CAC CTC ACC AAG GCC CAC  
Ile Val Leu Tyr Asn Asn Ala Asp Gly Asp Phe Ala Val Thr His Leu Thr Lys Ala His

CTG TTC TAT GAC GGA AGG GTG CAG TGG ACA CCC CCA GCC ATC TAT AAG AGC TCC TGC AGC  
Leu Phe Tyr Asp Gly Arg Val Gln Trp Thr Pro Pro Ala Ile Tyr Lys Ser Ser Cys Ser

ATC GAC GTC ACC TTC TTC CCG TTT GAC CAG CAG AAC TGT ACC ATG AAG TTT GGA TCC TGG  
Ile Asp Val Thr Phe Phe Pro Phe Asp Gln Gln Asn Cys Thr Met Lys Phe Gly Ser Trp

ACC TAC GAC AAG GCC AAG ATT GAC TTA GTG AGC ATT CAT AGC CGT GTG GAC CAA CTG GAC  
Thr Tyr Asp Lys Ala Lys Ile Asp Leu Val Ser Ile His Ser Arg Val Asp Gln Leu Asp

TTC TGG GAA AGT GGG GAG TGG GTC ATC GTG GAT GCT GTG GGC ACC TAC AAC ACC AGG AAG  
Phe Trp Glu Ser Gly Glu Trp Val Ile Val Asp Ala Val Gly Thr Tyr Asn Thr Arg Lys

TAC GAG TGC TGT GCC GAG ATC TAT CCT GAC ATC ACC TAT GCC TTC ATC ATC CGA CGC CTG  
Tyr Glu Cys Cys Ala Glu Ile Tyr Pro Asp Ile The Tyr Ala Phe Ile Ile Arg Arg Leu

CCG CTA TTC TAC ACC ATC AAC CTC ATC ATC CCG TGC CTG CTC ATC TCC TGT CTC ACC GTG  
Pro Leu Phe Tyr Thr Ile Asn Leu Ile Ile Pro Cys Leu Leu Ile Ser Cys Leu Thr Val

FIG. 2A-1



790 810 830  
CTG GTC TTC TAT CTG CCT TCA GAG TGT GGC GAG AAG GTC ACA CTG TGC ATC TCG GTG CTG  
Leu Val Phe Tyr Leu Pro Ser Glu Cys Gly Glu Lys Val Thr Leu Cys Ile Ser Val Leu

850 870 890  
CTT TCT CTC ACC GTC TTC CTG CTG CTC ATC ACC GAG ATC ATC CCG TCC ACC TCG CTG GTG  
Leu Ser Leu Thr Val Phe Leu Leu Leu Ile Thr Glu Ile Ile Pro Ser Thr Ser Leu Val

910 930 950  
ATC CCG CTC ATC GGC GAG TAC CTC CTC TTC ACC ATG ATC TTC GTC ACC CTC TCC ATC GTG  
Ile Pro Leu Ile Gly Glu Tyr Leu Leu Phe Thr Met Ile Phe Val Thr Leu Ser Ile Val

970 990 1010  
ATC ACG GTC TTC GTG CTC AAT GTG CAC CAC CCG TCG CCA CGC ACA CAC ACG ATG CCC GCC  
Ile Thr Val Phe Val Leu Asn Val His Cys Arg Ser Pro Arg Thr His Thr Met Pro Ala

1030 1050 1070  
TGG GTG CGT AGA GTC TTC CTG GAC ATC GTG CCT CGC CTC CTC TTC ATG AAG CGC CCC TCT  
Trp Val Arg Arg Val Phe Leu Asp Ile Val Pro Arg Leu Leu Phe Met Lys Arg Pro Ser

1090 1110 1130  
GTG GTC AAA GAC AAC TGC CGG AGA CTT ATT GAG TCC ATG CAC AAG ATG GCC AAC GCC CCC  
Val Val Lys Asp Asn Cys Arg Arg Leu Ile Glu Ser Met His Lys Met Ala Asn Ala Pro

1150 1170 1190  
CGC TTC TGG CCA GAG CCT GTG GGC GAG CCC GGC ATC TTG AGT GAC ATC TGC AAC CAA GGT  
Arg Phe Trp Pro Glu Pro Val Gly Glu Pro Gly Ile Leu Ser Asp Ile Cys Asn Gln Gly

1210 1230 1250  
CTG TCA CCT GCC CCA ACT TTC TGC AAC CCC ACG GAC ACA GCA GTC GAG ACC CAG CCT ACG  
Leu Ser Pro Ala Pro Thr Phe Cys Asn Pro Thr Asp Thr Ala Val Glu Thr Gln Pro Thr

1270 1290 1310  
TGC AGG TCA CCC CTT GAG GTC CCT GAC TTG AAG ACA TCA GAG GTT GAG AAG GCC AGT  
Cys Arg Ser Pro Pro Leu Glu Val Pro Asp Leu Lys Thr Ser Glu Val Glu Lys Ala Ser

1330 1350 1370  
CCC TGT CCA TCG CCT GGC TCC TGT CCT CCA CCC AAG AGC AGC AGT GGG GCT CCA ATG CTC  
Pro Cys Pro Ser Pro Gly Ser Cys Pro Pro Pro Lys Ser Ser Ser Gly Ala Pro Met Leu

1390 1410 1430  
ATC AAA GCC AGG TCC CTG AGT GTC CAG CAT GTG CCC AGC TCC CAA GAA GCA GCA GAA GAT  
Ile Lys Ala Arg Ser Leu Ser Val Gln His Val Pro Ser Ser Gln Glu Ala Ala Glu Asp

1450 1470 1490  
GGC ATC CGC TGC CGG TCT CGG AGT ATC CAG TAC TGT GTT TCC CAA GAT GGA GCT GCC TCC  
Gly Ile Arg Cys Arg Ser Arg Ser Ile Gln Tyr Cys Val Ser Gln Asp Gly Ala Ala Ser

1510 1530 1550  
CTG GCT GAC AGC AAG CCC ACC AGC TCC CCG ACC TCC CTG AAG GCC CGT CCA TCC CAG CTT  
Leu Ala Asp Ser Lys Pro Thr Ser Ser Pro Thr Ser Leu Lys Ala Arg Pro Ser Gln Leu

FIG.2A-2



1570 1590 1610  
CCC GTG TCA GAC CAG GCC TCT CCA TGC AAA TGC ACA TGC AAG GAA CCA TCT CCT GTG TCC  
Pro Val Ser Asp Gln Ala Ser Pro Cys Lys Cys Thr Cys Lys Glu Pro Ser Pro Val Ser

1630 1650 1670  
CCA GTC ACT GTG CAC AAG GCG GGA GGC ACC AAA GCA CCT CCC CAA CAC CTG CCC CTG TCA  
Pro Val Thr Val Leu Lys Ala Gly Gly Thr Lys Ala Pro Pro Gln His Leu Pro Leu Ser

1690 1710 1730  
CCA GCC CTG ACA CGG GCA GTA GAA GGC GTC CAG TAC ATT GCA GAC CAC CTC AAG GCA GAA  
Pro Ala Leu Thr Arg Ala Val Glu Gly Val Gln Tyr Ile Ala Asp His Leu Lys Ala Glu

1750 1770 1790  
GAC ACT GAC TTC TCG GTG AAG GAG GAC TGG AAA TAC GTG GCC ATG GTC ATT GAC CGA ATC  
Asp Thr Asp Phe Ser Val Lys Glu Asp Trp Lys Tyr Val Ala Met Val Ile Asp Arg Ile

1810 1830 1850  
TTC CTC TGG ATG TTC ATC ATT GTC TGC CTT CTG GGC ACT GTG GGA CTC TTC CTG CCT CCC  
Phe Leu Trp Met Phe Ile Ile Val Cys Leu Lue Gly Thr Val Gly Leu Phe Leu Pro Pro

1870 1890 1917  
TGG CTG GCT GCT TGC TGA TGGCTTCGACA GTTCTCAGGCTCAGTCTCCTGCTGACTTTGTTTCCAG  
Trp Leu Ala Ala Cys

1943 1969 1997  
TTTCTTCTCCGACAAAGTTGGCCTCCCTTCATTTATTCCTGTTATTTGGGCTTCGTGTTATTAATATCCTTCCCTGCC  
TCTGTGGCGCATTGTAAGTTTAAAAATTAATAGACCAAAGCC...3'

4-2 cDNA: 3' end  
↓  
1867 1884 1912  
CCC TGG CTG GCT GGT ATG ATC TAG GGACGTGGTGGTGCCAGCTCCACATCTCTGTAGGGCCATAC  
Pro Trp Leu Ala Gly Met Ile

1937 1963 1991  
GACTCGTCAGTCAACCCACATCTTCCAACCGGCTGACCATGAGACACCCTAGGAGAGAGATGATGCTTCTTGGGAGATG

2016 2042 2070  
GAAGTTGGCCCTGTTCTAGTCAGACTATGGGCGTGGTTGGAGAGAAATGAGGGCTGATACAGTTGCAGGCCGAGTCCC

2095 2121 2149  
CATTAAAGTTTCTCCAGAGCAAGTGGCAGTACTCCCTGACTTACAGACAGCACACCCCATCTGTGTACAGAGAATGA

2174 2200 2228  
TCCCGAGTTGATCTCAGTTGTCCTTTGAGGCCATGAAAAATTCATCCACCTTGAGGAACCCAGAGCCTCTCATGCTGTGG

2253 2279 2307  
GATCAATAAGACCAGGAATCTCCACTGTGACTCTGCTGGCCACACCCTCTCCCTCCCCAAGAAGTGGTCCCTCATCC  
CCCAATTC...3'

FIG.2A-3



ATAAAGTCTCCGGCAGTTGCTTTTGACACAGAGGGACGAGCGGCGCGCGGATGAAAGTTGGGTGCGCGCAGCTTCGGAGCGGAGGCGCGGCACAGCGCGGCGGCA-120  
-150  
-180  
-210

Met Glu Ile Gly Gly Pro Gly Ala Pro Pro Pro Leu Leu Leu Leu Leu Leu Leu Gly Thr  
ATG GAG ATC GGG GGC CCC GCG CCG CCG CCG CTG CTA CTG CCG CTG CTG CTC CTA GGG ACC

-90 -60 -30 -10

Glys Leu Leu Pro Ala Ser Ser His Ile Glu Thr Arg Ala His Ala Glu Glu Arg Arg Leu Lys Arg Leu Phe Ser Gly Tyr Asn Lys Trp  
 GGC CTC TTG CCT GCT AGC AGC CAC ATA GAG ACC CGG GCC CAT GCG GAG GAG GAG CGG CTC CTG AAG AGA CTC TTC TCC GGT TAC AAC AAG TGG  
 -1 1 1 1 10 10 20 60

Ser Arg Pro Val Gly Asn Ile Ser Asp Val Val Leu Val Arg Phe Gly Leu Ser Ile Ala Gln Leu Ile Asp Val Asp Glu Lys Asn Gln  
 TCT CGG CCA GTA GGC AAT ATC TCA GAT GTG GTC CTC CTC GTC CGC TTT GGC TTG TCC ATT GCT CAG CTC ATT GAC GTG GAC GAG AAC CAG

[illegible]

Arg Ile Pro Ser Glu Leu Ile Trp Arg Pro Asp Ile Val Leu Tyr Asn Ala Asp Gly Asp Phe Ala Val Thr His Leu Thr Lys Ala  
 C6C ATC CCC TCT GAA CTC ATC TGG AGG CCT GAC ATC GTC CTC TAC AAC AAT GCG GAT GGA GAC TTT GCA GTC ACC CAC CTG ACC ANG GCC  
 90 100 110 330 300 270

120  
 His Leu Phe Tyr Asp Gly Arg Val Gln Trp Thr Pro Pro Ala Ile Tyr Lys Ser Ser Cys Ser Ile Asp Val Thr Phe Phe Pro Phe Asp  
 CAC CTG TTC TAT GAC GGA AGG GTG CAG TGG ACA CCC CCA GCC ATC TAT TAT AAG AGC TCC TGC AGC ATC TTC TTC CCC TTT TTT GAC  
 360  
 130  
 390  
 420

Gln Gln Asn Cys Thr  
 CAG CAG AAC ACC TGT ACC  
 150  
 Met Lys Phe Gly Ser Trp Thr Tyr Asp Lys Ala Lys  
 ATG AAG TTT GGA TCC TGG ACC TAC GAC AAG GCC AAG  
 160  
 Val Asp Gln Leu  
 GTG GAC CAA Gln  
 170  
 Ser Arg Val Asp Gln  
 AGC CGT GTG GAC CAA Gln  
 510

FIG. 2B-1



180 Asp Phe Trp Glu Ser 190 Tyr Asn Thr Arg Lys Tyr Glu Cys Cys 200 Glu Ile Tyr Pro  
 GAC TTC TGG GAA AGT 540 TAC AAC ACC AGG AAG TAC GAG TGC TGT 600 GCC GAG ATC TAT CCT  
 210 Asp Ile Thr Tyr Ala Phe 220 Ile Asn Leu Ile Ile Pro Cys Leu Leu 230 Ser Cys Leu Thr  
 GAC ATC ACC TAT GCC 630 ATC CGA CGC CTG CCG CTA TTC TAC 660 ACC ATC AAG CTC ATC CCG TGC CTC ACC 690  
 240 Val Leu Val Phe Tyr 250 Cys Ile Ser Val Leu Leu Ser Leu Thr 260 Phe Leu Leu Leu  
 GTG CTG GTC TTC TAT 720 Pro Ser Glu Cys Gly Glu Lys Val Thr 750 Leu Cys TGC ATC TCG GTC CTG CTT TCT CTC ACC 780  
 270 Ile Thr Glu Ile Ile 280 Glu Tyr Leu Leu Phe Thr Met Ile Phe 290 Thr Leu Ser Ile  
 ATC ACC GAG ATC ATC 810 Ser Thr Ser Leu Val Ile Pro Leu Ile 840 Gly GAG TAC TAC CTC CTC TTC ACC ATG ATC TTC 870  
 300 Val Ile Thr Val Phe Val 310 His Thr Met Pro Ala Trp Val Arg Arg 320 Phe Leu Asp Ile  
 GTC ATC ACC GTC TTC 900 Leu Asn Val His His Arg Ser Pro Arg Thr 930 CAC CAC CCG TCG CCA CGC 960 GTC TTC CTG GAC ATC  
 330 Val Pro Arg Leu Leu 340 Met Lys Arg Pro Ser Val Val Lys Asp 350 Met Ala Asn Ala  
 GTG CCT CGC CTC CTC 990 ATG AAG CGC CCC TCT GTG GTC AAA GAC 1020 TGC CGG AGA CTT ATT GAG TCC TCC ATG CAC AAG ATG GCC AAC GCC  
 360 Pro Arg Phe Trp Pro 370 Ile Cys Asn Gln Gly Leu Ser Pro Ala 380 Thr Phe Cys Asn  
 CCC CGC TTC TGG CCA 1080 CCT GTG GGC GAG CCC GGC ATC TTG AGT 1110 GAC ATC TGC AAC CAA GGT CTG TCA CCT GCC CCA ACT TTC TGC AAC  
 390 Pro Thr Asp Thr Ala Val 400 Leu Glu Val Pro Asp Leu Lys Thr Ser 410 Val Glu Lys Ala  
 CCC ACG GAC ACA GCA 1170 Glu Thr Gln Pro Thr Cys Arg Ser Pro Pro 1200 CTT GAG GTC CCT GAC TTG AAG ACA TCA GAG GTT GAG AAG GCC  
 1230

FIG.2B-2



420 Ser Pro Cys Pro Ser Glu Ser Cys Pro Pro Lys Ser Ser Ser 430 Leu Ser Val Gln  
AGT CCC TGT CCA TCG CCT GGC TCC TGT TGT CCA CCC AAG AGC AGC AGC TCC TCC CTG AGT GTC GGC  
1260  
450 His Val Pro Ser Ser Glu Ala Ala Asp Gly Ile Arg Cys Arg 460 Asp Gln  
CAT GTG CCC AGC TCC CAA GAA GCA GAA GAT GGC ATC CGC TGC CGG TCT CGG AGT ATC CAG TAC TGT GTT TCC  
1350  
480 Ser Leu Ala Asp Ser Lys Pro Thr Ser Ser Pro Thr Ser Leu Lys Ala Arg 490 Ala Ser Pro Cys  
TCC CTG GCT GAC AGC AAG CCC ACC AGC TCC CCG ACC TCC TCC CCG TCC CAG CTT CCC GTG TCA GAC GGC TCT CCA TGC  
1440  
510 Lys Cys Thr Cys Lys Glu Pro Ser Pro Val Thr Val Leu 520 His Leu Pro Leu  
AAA TGC ACA TGC ANG GAA CCA TCT CCT CCT GTG TCC CCA GTC ACT GTG CTC ANG GCG GGA GGC ACC AAA GCA CCT CCC CAA  
1530  
540 Ser Pro Ala Leu Thr Arg Ala Val Glu Gly Val Gln Tyr Ile Ala Asp 550 Ser Val Lys Glu Asp  
TCA CCA GCC CTG ACA CGG GCA GTA GAA GAA GGC GTC CAG TAC TAC ATT GCA GAC CAC CTC AAG GCA GAA GAC ACT GAC TTC TCG  
1620  
570 Trp Lys Tyr Val Ala Met Val Ile Asp Arg Ile Phe Leu Trp Met Phe 580 Gly Leu Phe Leu Pro  
TGG AAA TAC GTG GCC ATG GTC ATT GAC CGA ATC TTC CTC TGG ATG TTC ATC ATC ATT GTC TGC CTT CTG GGC ACT GTC GGA CTC  
1710  
600 Pro Trp Leu Ala Gly Met Ile TAG GGACGTGGTGGTGCCAGCTCCACATCTCTGTAGGGCCCATACGACTCGTCAGTCCACCCACATCTTCCAAACCGGCTGACCAATGAG  
CCC TGG CTG GCT GGT ATG ATC TAG 1800  
ACACCCTAGGAGAGAGATGATGCTTCTTGGGAGATGGAAGTTGGCCCTGGTTCTAGTCAGACTATGGCGGTGGTTGGAGAGAAATGAGGGCTGATACAGTTGCAGGCCGAGTCCCCCAT  
1920 1950 1980 2010

FIG.2B-3

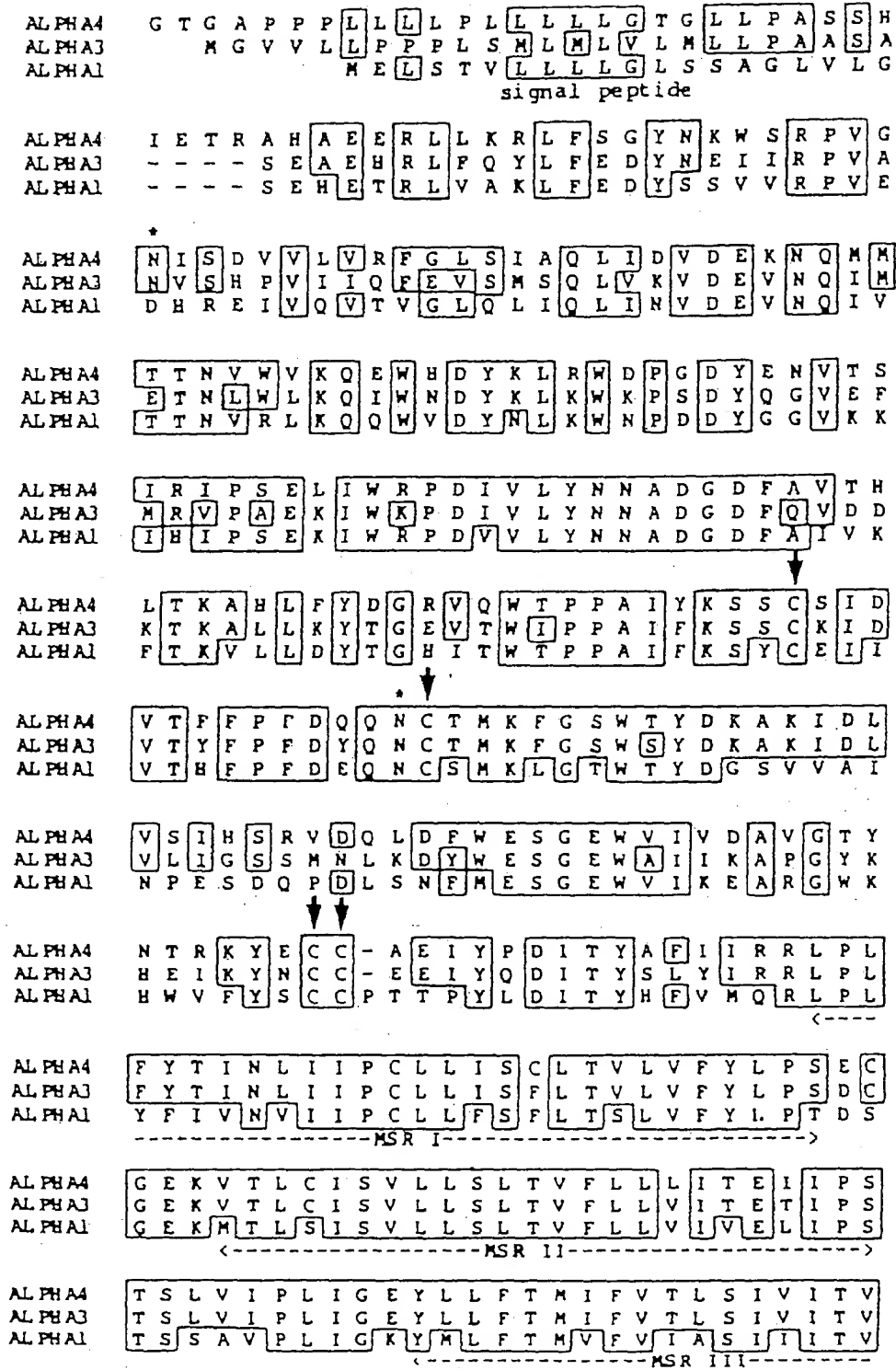


FIG.3A





ALPHA4 F V L N V H H R S P R T H T M P A W V R R V F L D I V  
ALPHA3 F V L N V H Y R T P T T H T M P T W V K A V F L N L L  
ALPHA1 I V I N T H H R S P S T H I M P E W V R K V F I D T I  
----->

ALPHA4 P R L L F - - - M K R P S V V K D N C R R L I E S M H  
ALPHA3 P R V M F - - - M T R P T S G E G D T P K T - - - -  
ALPHA1 P N I M F F S T M K R P S R D K Q E K R I F - - - -

ALPHA4 X M A N A P R F W P E P V G E P G I L S D I C N Q G L  
ALPHA3 - - - - - - - - - - R T F Y G A E L S N L N C F S R  
ALPHA1 - - - - - - - - - - T E D I D I S D I S G K P G

ALPHA4 S P A P T F C N P T D T A V E T Q P T C R S P P L E V  
ALPHA3 A D S K S C K E G Y P C O D G T C G Y C H H R R V K I  
ALPHA1 P P P M G F H - - - - - - - - - - - - - - - - - -

ALPHA4 P D L K T S E V E K A S P C P S P G S C P P P K S S S  
ALPHA3 S N F - - - - - - - - - - - - - - - - - - S A N L T R S S S  
ALPHA1 -

ALPHA4 G A P M L I K A R S L S V Q H V P S S Q E A A E D G I  
ALPHA3 S E S V -  
ALPHA1 -

ALPHA4 R C R S R S I Q Y C V S Q D G A A S L A D S K P T S S  
ALPHA3 -  
ALPHA1 -

ALPHA4 P T S L K A R P S Q L P V S D Q A S P C K C T C K E P  
ALPHA3 -  
ALPHA1 -

ALPHA4 S P V S P V T V L K A G G T K A P P Q H L P L S P A L  
ALPHA3 - - - - - - - - - - - - - - - - - - N A V L S L S A L S P E I  
ALPHA1 - - - - - - - - - - - - - - - - - - S P L I K H P E V  
-----<

ALPHA4 T R A V E G V Q Y I A D H L K A E D T D F S V K E D W  
ALPHA3 K E A I Q S V K Y I A E N M K A Q N V A K E I Q D D W  
ALPHA1 K S A I E G V K Y I A E T M K S D Q E S N N A A E E W  
amphipathic helix----->

ALPHA4 K Y V A M V I D R I F L W M F I I V C L L G T V G L F  
ALPHA3 K Y V A M V I D R I F L W V F I L V C I L G T A G L F  
ALPHA1 K Y V A M V M D H I L L L G V F M L V C L I G T L A V F  
-----<-----MSR IV----->

ALPHA4 L P P W L A G M I  
ALPHA3 L Q P L M A - R D D T  
ALPHA1 A G R L I E L H Q Q G  
-->

FIG.3B

FIG.4A

Clone 4-1;  
Antisense

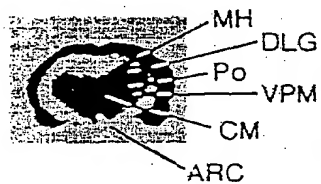
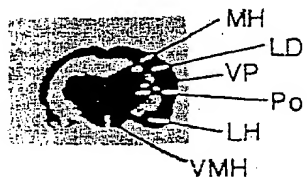
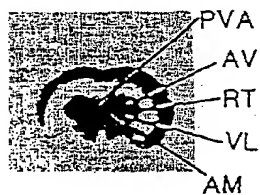


FIG.4B

Clone 4-1;  
Sense

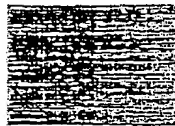
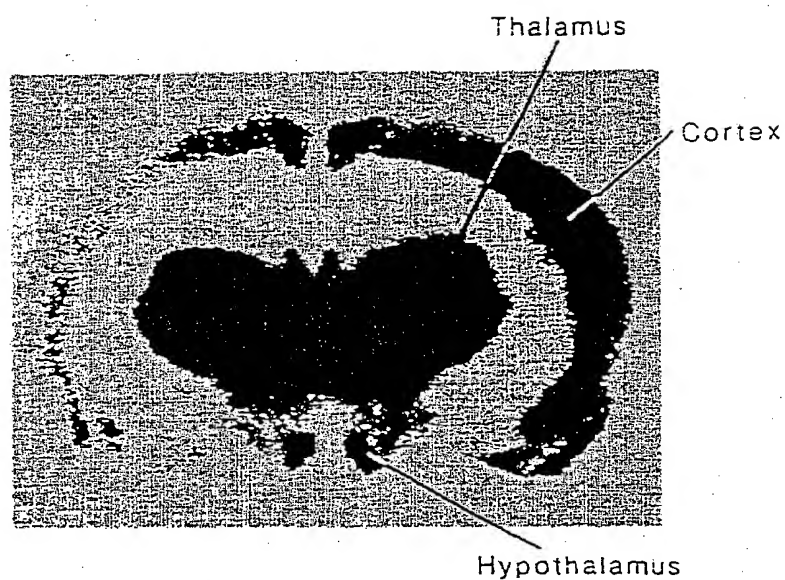


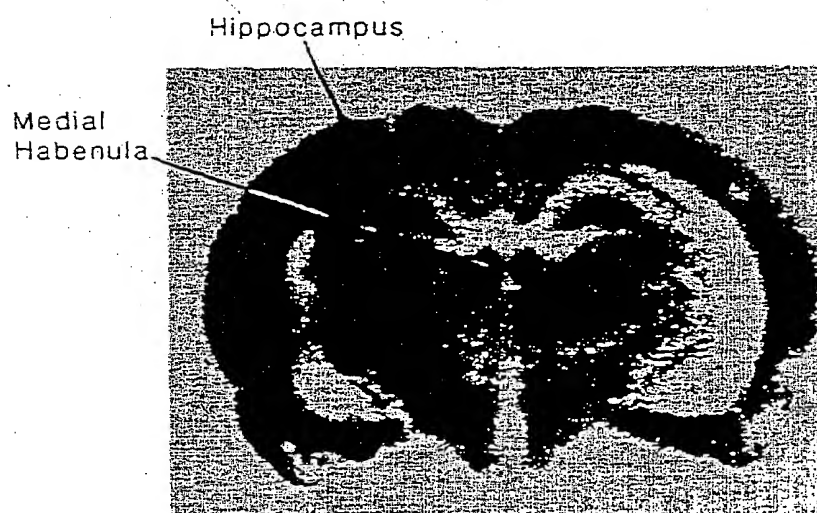


FIG.5A



PROBE: Alpha 4

FIG.5B



PROBE: Alpha 3

FIG.6A

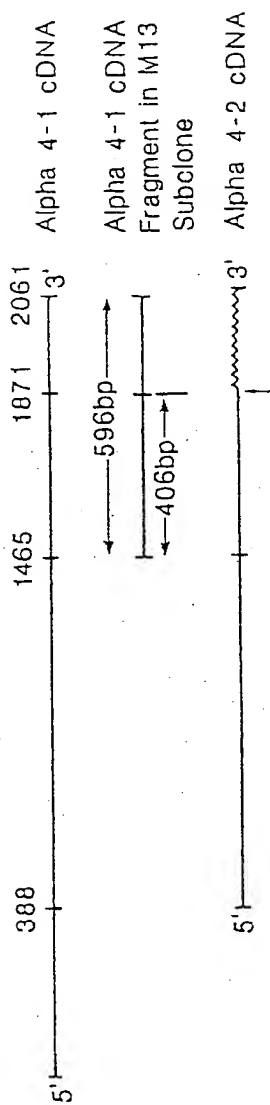


FIG.6B

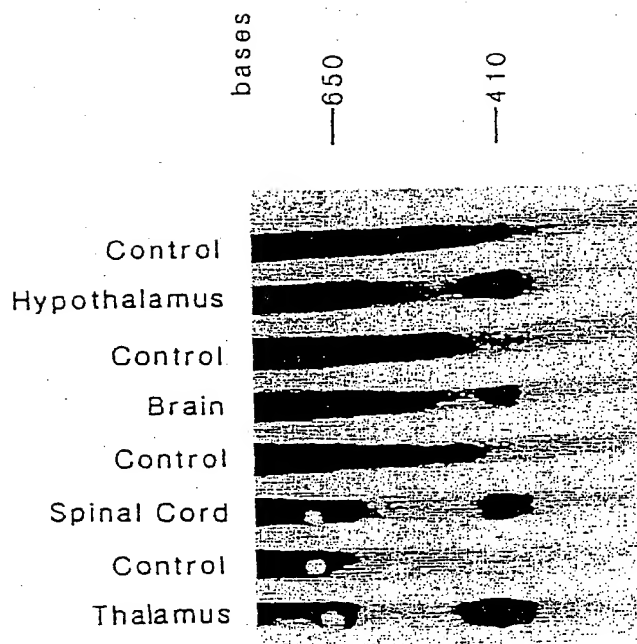
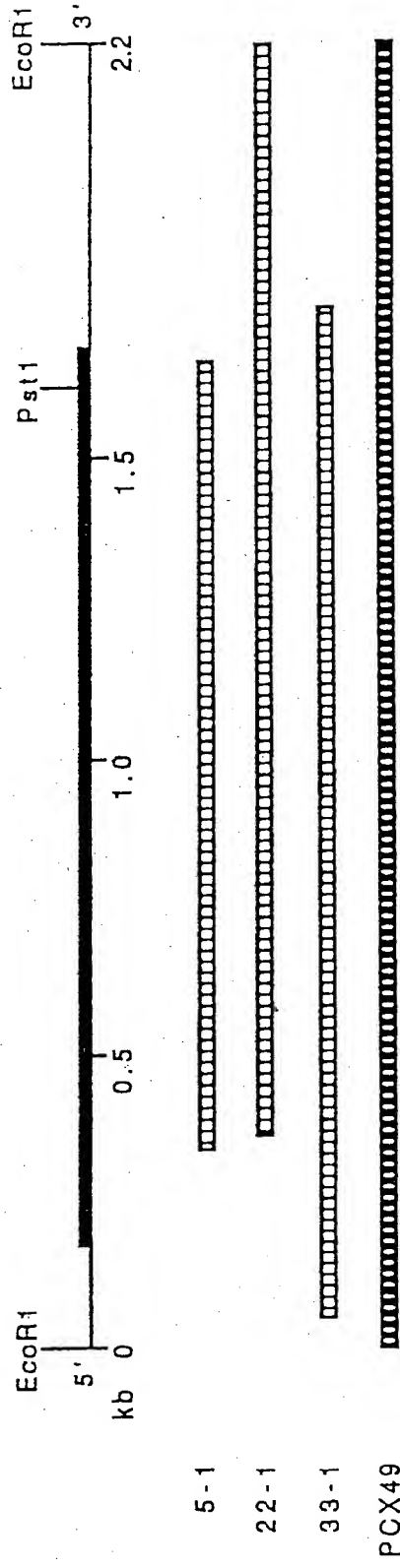
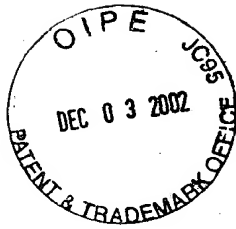




FIG.7A





5' ..... -179 -100  
TGGAGGCGGAGCCCAACCCGGGACCGGCAAGAGCCGGGACCTCCCTCGTTGCAGGAAGTCCCGGTTTCAGTGAGCACACCTTTAGACC  
Met Leu Ala Cys Met Ala Gly His Ser Asn Ser Met Ala Leu Phe Ser Phe Ser Leu Leu Trp Leu Cys Ser Gly  
GTT TTG GGA ACT GAC ACA GAG GAG CTA GTG GAG CAT CTC TTA GAT CCC TCC CGC TAT AAC AAG CTG ATT CGT  
Val Leu Gly Thr Asp Thr Glu Glu Arg Leu Val Glu His Leu Leu Asp Val Ser Arg Tyr Asn Lys Leu Ile Arg  
CCA GCT ACT AAC GGC TCT GAG CTG GTG ACT GTA CAG CTC ATG GTA TCA TTG GCT CAG CTC ATT AGT GTG CAC GAG  
Pro Ala Thr Asn Gly Ser Glu Leu Val Thr Val Glu Leu Met Val Ser Leu Ala Gln Leu Ile Ser Val His Glu  
CGG GAG CAG ATC ATG ACC ACC AAT GTC TGG CTG ACC CAG GAG TGG GAA GAT TAC CGC CTC ACA TGG AAG CCT GAG  
Arg Glu Gln Ile Met Thr Thr Asn Val Thr Leu Thr Gln Glu Trp Glu Asp Tyr Arg Leu Thr Trp Lys Pro Glu  
GAC TTC GAC AAT ATG AAG AAA GTC CGG CTC CCT TCC AAA CAC ATC TGG CTC CCA GAT GTG GTT CTA TAC AAC AAT  
Asp Phe Asp Asn Met Lys Lys Val Arg Leu Pro Ser Lys His Ile Trp Leu Pro Asp Val Val Leu Tyr Asn Asn  
GCT GAC GGC ATG TAC GAA GTC TCC TTC TAT TCC AAT GCT GTG GTC TCC TAT GAT GGC AGC ATC TTT TGG CTA CCA  
Ala Asp Gly Met Tyr Glu Val Ser Phe Tyr Ser Asn Ala Val Val Ser Tyr Asp Gly Ser Ile Phe Trp Leu Pro  
CCT GCC ATC TAC AAG AGT GCA TGC AAG ATT GAG GTG AAG CAC TTC CCA TTT GAC CAG CAG AAT TGC ACC ATG AAG  
Pro Ala Ile Tyr Lys Ser Ala Cys Lys Ile Glu Val Lys His Phe Pro Phe Asp Gln Gln Asn Cys Thr Met Lys

FIG.7B-1

TTT CGC TCA TGG ACC	540	IAC GAC CGT ACT GAG ATT GAC CTG GTG	570	CTC AAA AGT GAT GTG GCC AGT CTG GAT GAC	600	TTC Phe Arg Ser Trp Thr	Tyr Asp Arg Thr Glu Ile Asp Leu Val	Leu Ser Ala Ser Leu Asp Asp Phe
ACA CCC AGC GGG GAG	630	TGG GAC ATC ATC GCA CTG CCA GGC CGA	660	GAC AAC GAG AAC CCA GAC GAC TCC ACC TAT	690	Thr Pro Ser Gly Glu Trp Asp Ile Ile Ala Leu Pro Gly Arg Arg	Asn Glu Asn Pro Asp Asp	Tyr Val
GAC ATC ACC TAT GAC	690	TTC ATC ATT CGT CGC AAA CCA CTC TTC	720	ACT ATC AAC CTC ATC ATC CCC TGC GTA	750	Asp Ile Thr Tyr Asp Phe Ile Ile Arg Arg Lys Pro Leu Lys Pro Leu	Thr Ile Asn Leu Ile Ile Pro Cys Val	Leu
ATC ACC TCG CTG GCC ATC	780	CTG TTC TAC TAC TAC TCA GAC TGT GGT GAA AAG ATG	810	ACA CTT TGT ATT TCT	840	Ile Thr Ser Leu Ala Ile Leu Val Phe Tyr Tyr	Met Thr	GTG
CTG CTA GCA CTC ACG	840	GTG TTC CTG CTG CTC ATC TCC AAG ATT GTG	870	CCT CCC ACC TCC CTC GAT GTG	900	Leu Leu Ala Leu Thr Val Phe Leu Leu Leu Ile Ser	Leu Asp Val Pro Leu Val	GTG
GGC AAG TAC CTC ATG	930	TTT ACC ATG GTG CTA GTC ACC TTC TCC ATC	960	GTC ACC AGC GTG TGT GTG CTC AAT GTG	990	Gly Lys Tyr Leu Met Phe Thr Met Val Leu Leu Val Thr Ser Val Cys Val	Leu Asn Val	CAC
CAC CGC TCG CCT ACC	990	ACG CAC ACC ATG GCC CCC TGG GTC AAG GTG	1020	GTC TTC CTG GAG AAG CTG CCC ACC CTG	1050	His Arg Ser Pro Thr Thr His Thr Met Ala Pro Trp Val Lys Val	Pro Thr Leu Leu	CTC
TTC CTG CAG CAG CCA	1080	CGC CAC CGC TGT GCA CGT CAG CGT TTG AGG	1110	CGC CAG CGA GAG CGT GAG	1140	Phe Leu Gln Gln Pro Arg Arg His Arg Cys Ala Arg Gln Arg	Arg Gln Arg Glu Arg	Gly

FIG.7B-2

1140 GAG GCG GTT TTC TTC CGT GAA GGT CCT GCG GCT GAC CCA TGT ACC TGC TTT GTG AAC CCT GCA TCA GTG CAG GGC 1200  
 Glu Ala Val Phe Phe Arg Glu Gly Pro Ala Ala Asp Pro Cys Thr Cys Phe Val Asn Pro Ala Ser Val Gln Gly  
 376  
 1230 TTG GCT GGG GCT TTC CGA GCT GAG CCC ACT GCA GCC GGC CCG GGG CGC TCT GTG GGG CCA TGC AGC TGT GGC CTC  
 Leu Ala Gly Ala Phe Arg Ala Glu Pro Thr Ala Ala Gly Pro Gly Arg Ser Val Gly Pro Cys Ser Cys Gly Leu  
 401  
 1290 CCG GAA GCA GTG GAT GGC GTA CCG TTC ATT GCG GAC CAC ATG CGA AGT GAG GAT GAT GAC CAG AGT GTG AGG GAG 1350  
 Arg Glu Ala Val Asp Gly Val Arg Phe Ile Ala Asp His Met Arg Ser Glu Asp Asp Gln Ser Val Arg Glu  
 428  
 1380 GAC TGG AAA TAC GTT GCC ATG GTG ATC GAC CGC CTG TTC CTG TGG ATC TTT GTG TTT GTG TGT GTC TTT GGG ACC  
 Asp Trp Lys Tyr Val Ala Met Val Ile Asp Arg Leu Phe Phe Val Phe Val Cys Val Phe Gly Thr  
 451  
 1440 GTC GGC ATG TTC CTG CAG CCT CTC TTC CAG AAC TAC ACT GCC ACT ACC TTC CTC CAC CCT GAC CAC TCA GCT CCC 1500  
 Val Gly Met Phe Leu Leu Pro Leu Phe Phe Thr Ala Thr Thr Phe Leu His Pro Asp His Ser Ala Pro  
 476  
 1596 AGC TCC AAG TGAGGTCATTCATTTTGCAGCTCCTCACCCCGTGACCCCTGCGGTTTCAGTACTGGGTGCAAGATGGATCTCTCCCCACTCCACTGA  
 Ser Ser Lys  
 501  
 1695 AGCCTGCTTACACACCTCCGTTACACACATAGTCTCCAGCCTGGAGGCTGGACCCGCTGCCTTGTGGTGGAGCCTTCTCCTTCCCTCTGAGCTCGTTCA  
 1794  
 GGCAGGAGTGCCAAATGGTGGGGGCCACCGGCTGGTAAGTAGAGGCCAGAGATCACAGAGCCACCTACCCCGATGAGGTGCTGGAGAGAGGCCCAAGAAAG  
 1893  
 AGACAGAGTTATCTGTGACCTCCAAGTCATCGGAGAGGAGGAGGTAGGATAAGGGGCTCAGACTCTGGCAGAGTGGGCTAGTACTTGGCGCCCA  
 1992  
 CTTAAGTGAGCGACACTGGTCTGGGAGGACTCGAAGTGTGGGAGCTCTCTTGGGAGCTCGGTCTCCACCCCTGTACCTCAGAGGGGCTCCAGACCCCGG  
 2017  
 GCTTCAGGTTCCCTTCTGCCAGTGC.....3'

FIG.7B-3



**FIG. 8**



FIG.9A

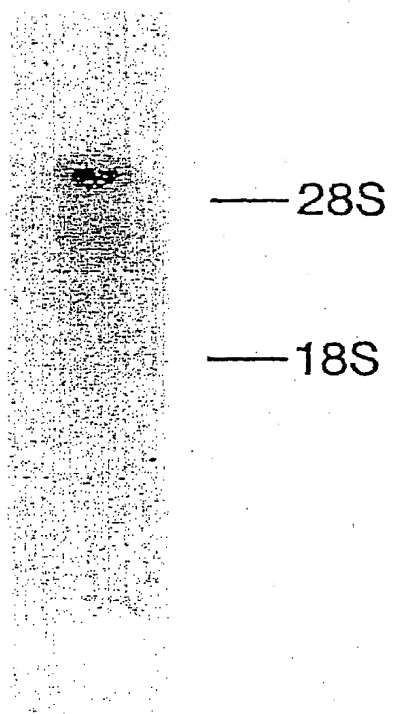


FIG.9B

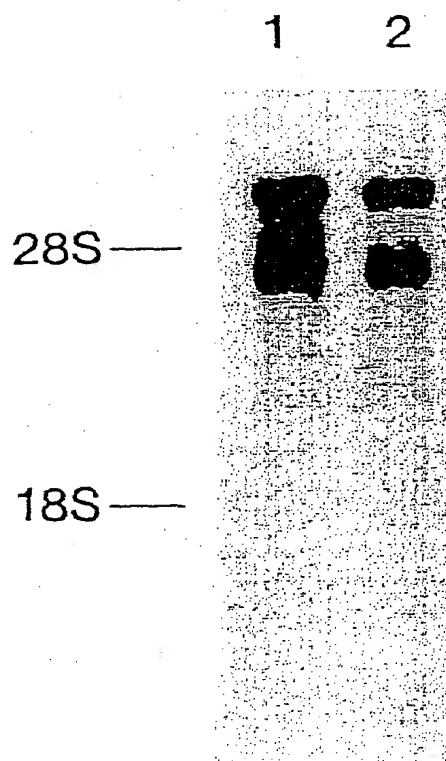


FIG. 10A  
ANTISENSE

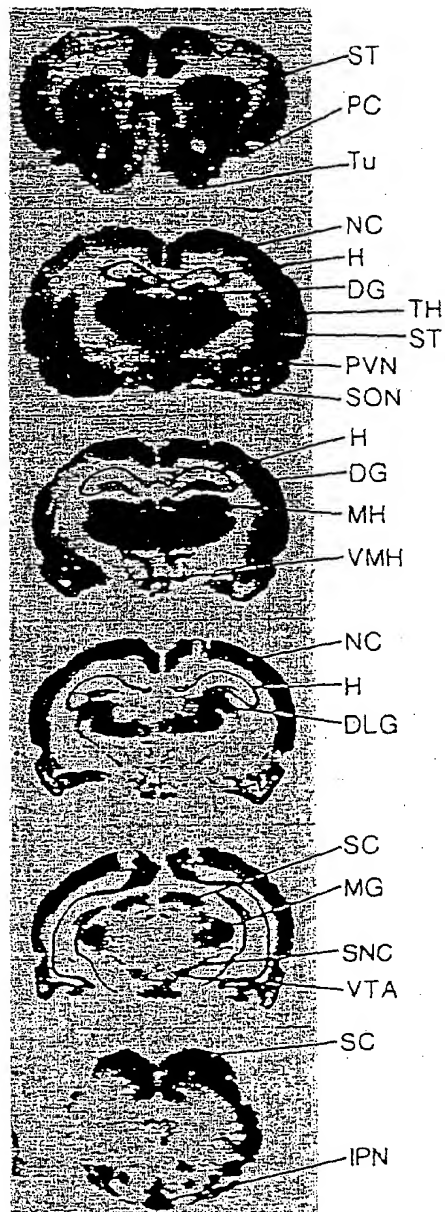
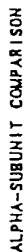


FIG. 10B  
SENSE





ALPHA 1 MELSTVLLLLGLSSAGLVGLSEHTITVAKVTEQDSSVVHVEDHREIDQVTVGLOLIDTIAVUIVDDIVTIVTVALVDQVDVITNINQVNDQDTGGCKKHILIPS  
 ALPHA 3 MGVVLLPPLPSNLMLVLMPLPAASAEAHHTFOYLLDEDNEIIPANVSHPTIQFVSSQLVYKVDVFOIMEITLLWLGINKTKCKKSTQDGEVEFARVPA  
 ALPHA 4 WANSGTGAPPLLLLLLTGGLPASHIETRAHGERIKRKLSSGKMKWSHMGVGNISDYLVRFGLSIADIDQDKVDVNTITVNVKYEENHDKIRADQDQTEANTSTRIDS  
 SIGNAL PEPTIDE

[illegible]

	MEMBRANE SPANNING I				MEMBRANE SPANNING II				MEMBRANE SPANNING III				
ALPHA 1	DIETHEFVQGNRYF	IVTV	ITPCLCT	EFETIS	VFTEPTOSTHRE	WTIS	SVITESTITUTLV	VF	TPSTESCAVPLTCK	PCPTDVSQVLA	ITPTQ	IVTITHTHSSST	INDVEMDKVF
ALPHA 2	DIETSLIRINVF	YTYL	ICPCLL	IFRIN	VFPLPSGGEM	ILC	SVLLSLIKVLLV	TEET	HPISLSLV	PLCELT	ITVLT	IVFVQVQVQV	ITTHSTWAKAT
ALPHA 3	DIETAFIRINVF	YTYL	ICPCLL	IFRIN	VFPLPSGGEM	ILC	SVLLSLIKVLLV	TEET	HPISLSLV	PLCELT	ITVLT	IVFVQVQVQV	ITTHSTWAKAT
ALPHA 4	DIETAFIRINVF	YTYL	ICPCLL	IFRIN	VFPLPSGGEM	ILC	SVLLSLIKVLLV	TEET	HPISLSLV	PLCELT	ITVLT	IVFVQVQVQV	ITTHSTWAKAT

ALPHA 1 IDTIDUIMJEFSTUKAPSDKOEKRIPTEDIDISIOGKPGPPUGFHH  
 ALPHA 2 LNNLHVRVUJTRTJSGEDTPKTRTFYGAELSNLHCFRADSKCKEYPCODGTGCGYCHHRRVKISFNSANLTRSSSESVMAYL  
 ALPHA 3 LNNLHVRVUJTRTJSGEDTPKTRTFYGAELSNLHCFRADSKCKEYPCODGTGCGYCHHRRVKISFNSANLTRSSSESVMAYL  
 ALPHA 4 LDIVJALLUJUKRPSVVDNCRRLIESUHKUNAPAFWPEVPGVGEILSDICHOGLSPATPCNPIDTAYETOPTCRSPPLEYDPLK7SEVEKASPCPSGSCPPKSSSSCAPMLIKA  
 CYTOLASMIC REGION

ALPHA 1  
 ALPHA 3  
 ALPHA 4  
 RSLSVOHVPSOEALEDGIRCRSRSIQCYSGDGAASLADSKPTSPSTSLKARPSQLPVSDQASCKCTCKEPPSPVPTVLKAGGTAKPPHPLPSLALTRAVGVDVINDHLKAE  
 SLSALSDEIKKAIQSKIPDENHQAQ  
 SPLIKHDEVKSAIEGKTYQETWISD  
 AMPHIPATHIC HELIX  
 CYTOPLASMIC REGION

ALPHA 1 QESNNAEEENVGR. HICGVHILKILFLAYVAGRLIELHQQG  
ALPHA 2 QESNNAEEENVGR. HICGVHILKILFLAYVAGRLIELHQQG  
ALPHA 3 NVAYEIQDFANVLD. IIRFVYVILKILFLAYVAGRLIELHQQG  
ALPHA 4 DTDFSVKEDKNSVGR. IIRFVYVILKILFLAYVAGRLIELHQQG

**FIG. 1**

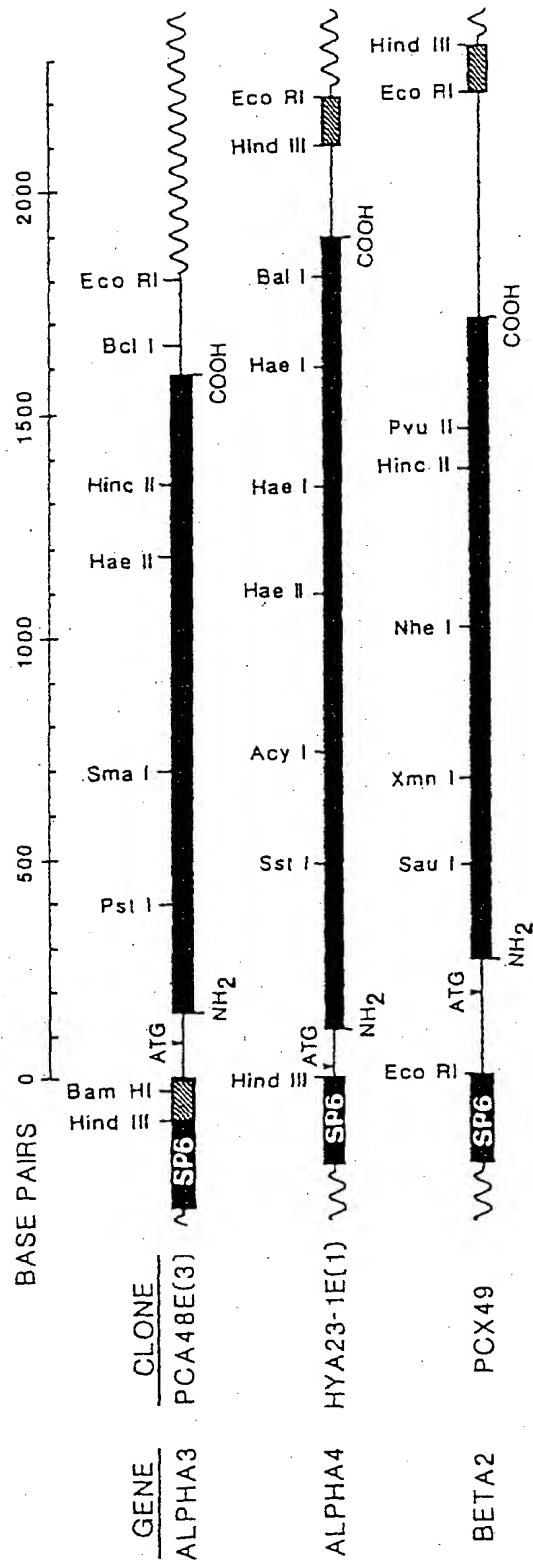


FIG.12

mRNAs injected	Responses to Acetylcholine (ACh)	Responses to Nicotine (Nic)
----------------	----------------------------------	-----------------------------

FIG.13A alpha3 + beta2

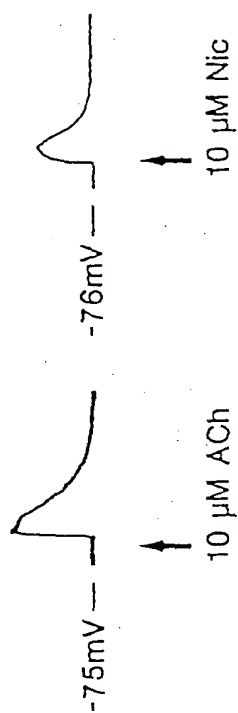


FIG.13B alpha4 + beta2

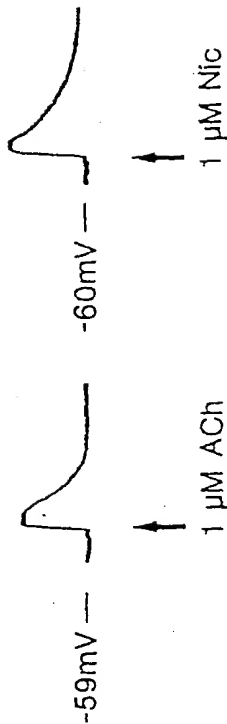
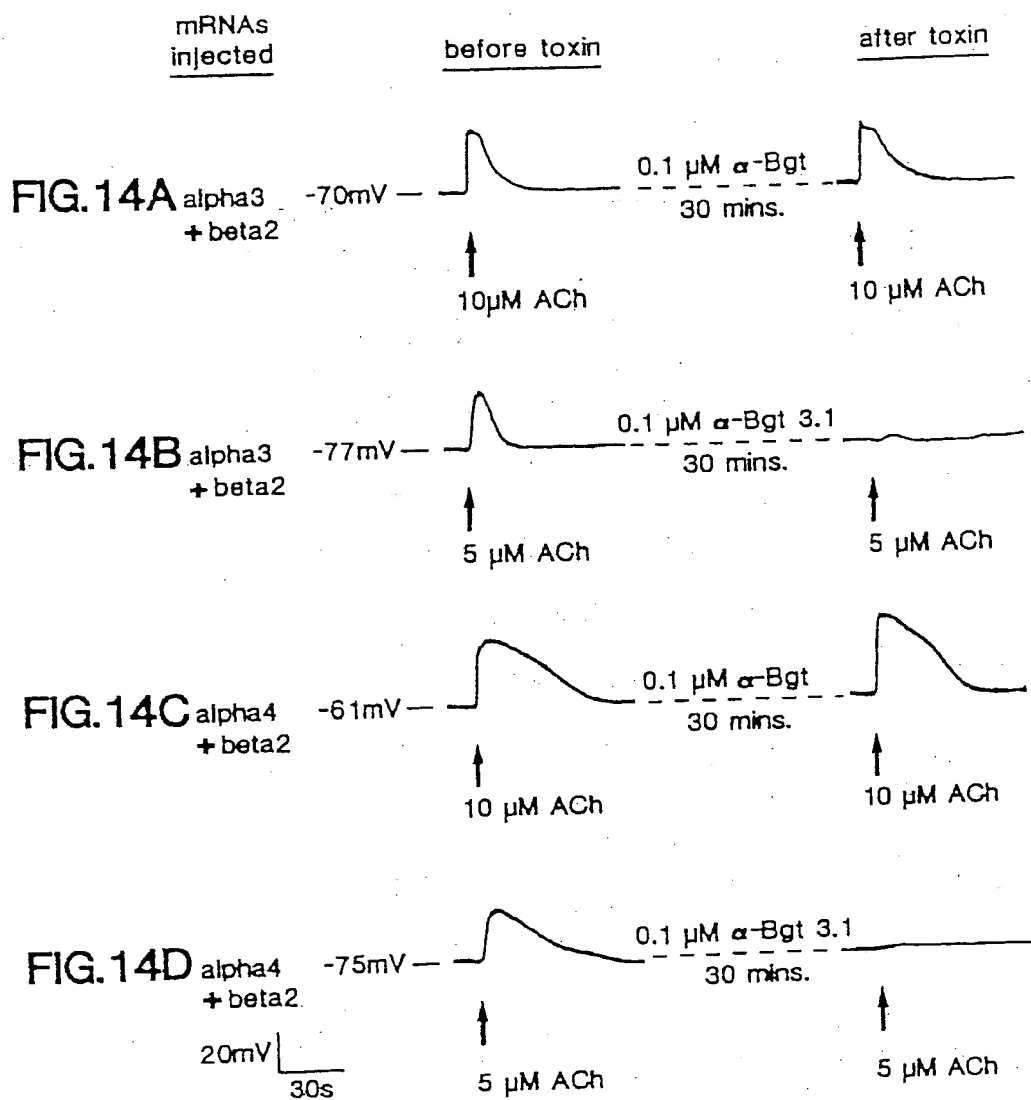


FIG.13C alpha4





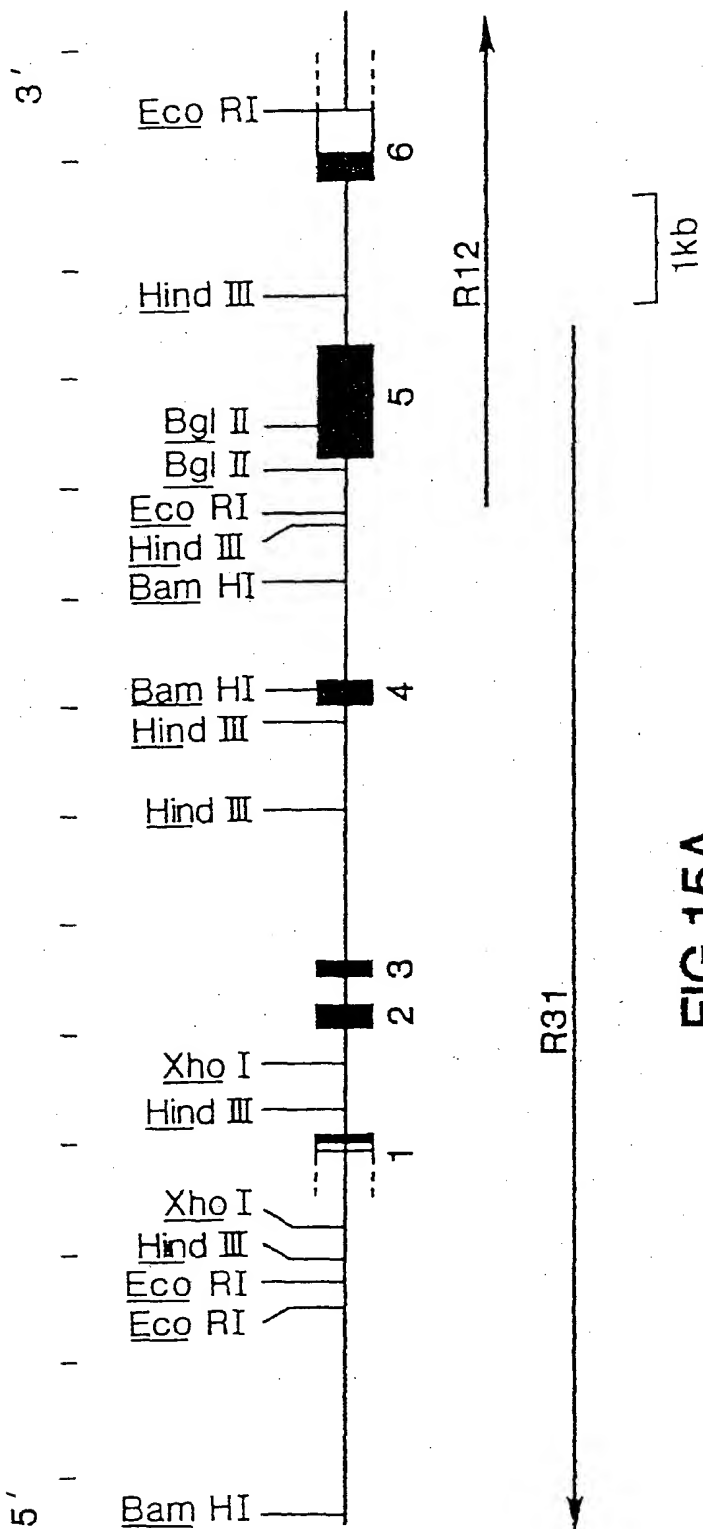
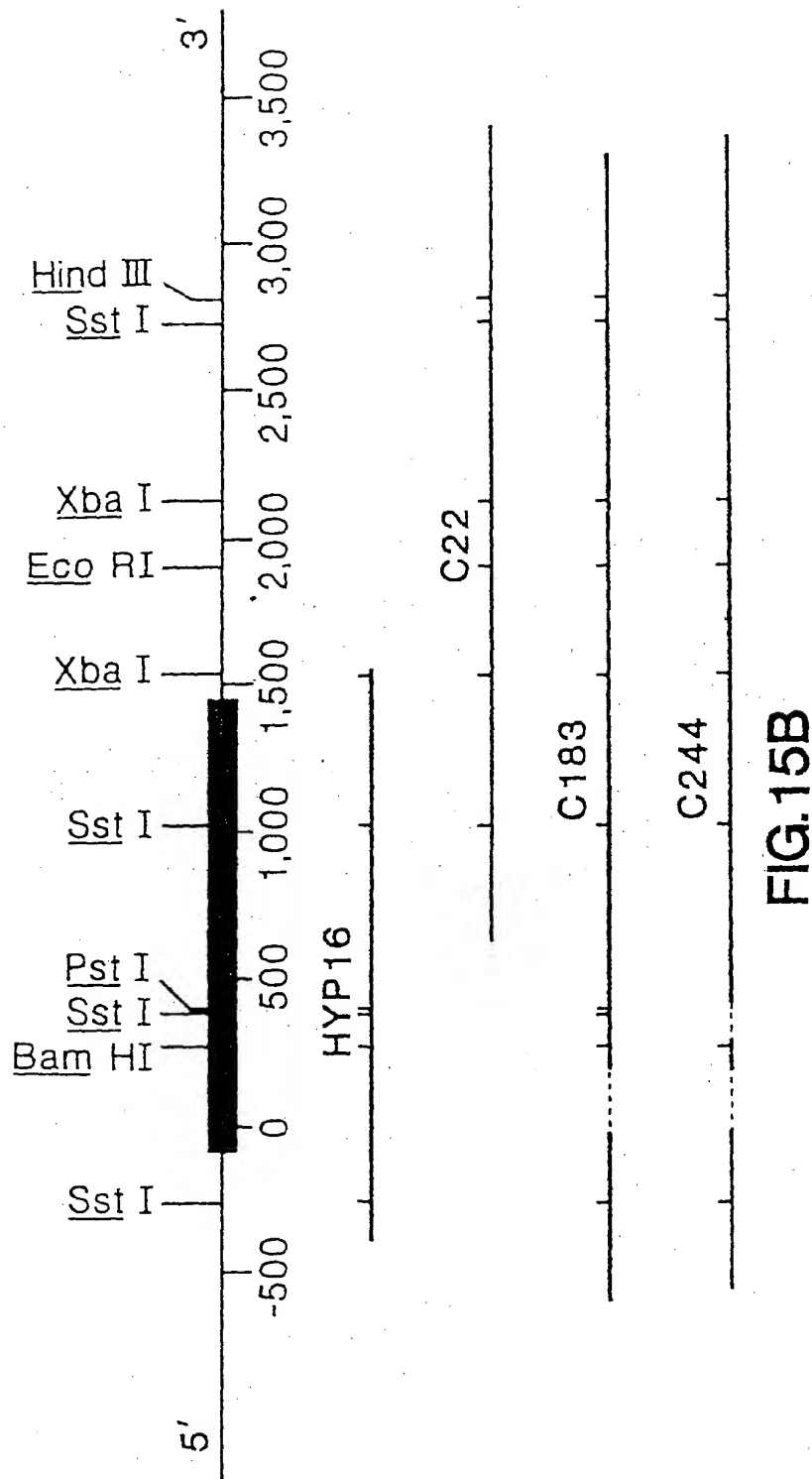


FIG.15A

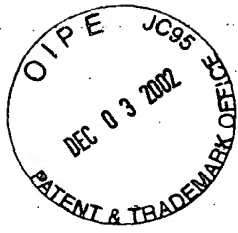






5'.....ACTGAGCATTC  
-360 TGTGAACTCGGATCACCTATCTCCAGGAAGCTAGCCTGAATCCCTCATCCCAACAGTGCCTCCCAACCTTGCAAGTTCTGTGTGGGCAACCATGAGCTGAAGCAACTGAGCTCTG  
-330  
-270  
TTCTGCACCTGTGCACIGCTTCCGAGGGACCCCTGCTCAGCCACCCAGGCTCTCCAGCGGTGGTTCTCTGCAATCCCTTGAGGGGCGCTGTCTTCTATGACAATTGCAGAGAGACAGT  
-240  
-180  
-150  
GCCTCAAAGAGCCAGCTCTTGGTAGTCCAGGGAAACAGGACCCCTCTGAGCC ATG ACC CTT TCC CAT TCT GCT CTC CAG TTC TGG ACA CAT CTT TAT CTC  
-120  
-90  
-60  
Met Thr Leu Ser His Ser Ala Leu 6ln Phe Trp Thr His Leu Tyr Leu  
-30  
TGG TGT CTC CTT CTG GTG CCA GCA G gtaagt.....tatccacacag TG TTG ACC CAG CAA GGC TCA CAC ACC CAT GCT GAG GAC CGC CTG TTC  
Trp Cys Leu Leu Val Pro Ala V al Leu Thr Gln Gln Gln Gly Ser His Thr His Ala Glu Asp Arg Leu Phe  
-10  
AAA CAC CTG TTT GGA GGC TAC AAT CGC TGG GCA CGG CCA GTG CCC AAC ACT TCT GAT GTG GTC ATC GTG CGC TTT GGA TTA ICC ATT GCT  
Lys His Leu Phe Gly Gly Tyr Asn Arg Trp Ala Arg Pro Val Pro Asn Thr Ser Asp Val Val Ile Val Arg Phe Gly Leu Ser Ile Ala  
60  
CAG CTC ATA GAT GTG gtgggc.....gctacaacag GAT GAG AAG AAT CAA ATG ATG ACC ACC AAT GTC TGG CTA AAG CAG gtaaac.....  
Gln Leu Ile Asp Val Asp Glu Lys Asn Gln Met Met Thr Thr Asn Val Trp Leu Lys Gln  
150  
210  
.....ccctaagcag GAA TGG AAT GAC TAC AAG CTG CGC TGG GAC CCG GCT GAG TTT GGC AAT GTG ACC TCC CTG CGC GTC CCT TCA GAG ATG  
Glu Trp Asn Asp Tyr Lys Leu Arg Trp Asp Pro Ala Glu Phe Gly Asn Val Thr Ser Leu Arg Val Pro Ser Glu Met  
70  
80

FIG.15C-1



270 ATC TGG ATC CCA GAC ATT GTC CTC TAC AAC AA gtaaga.....ctcttccag T 300 GCA GAT GGG GAG TTT GCG GTG ACC CAC ATG ACC AAG  
 Ile Trp Ile Pro Asp Ile Val Leu Tyr Asn As 100 n Ala Asp Gly Glu Phe Ala Val Thr His Met Thr Lys  
 90  
 GCT CAC CTC TTC TTC ACG GGC ACT GTG CAC TGG GTG CCC CCA GCC ATC TAC AAG AGC TCC TGC AGC ATC GAT GTG ACC TTC TTC CCC TTC  
 Ala His Leu Phe Phe Thr Gly 120 Val His Trp Val Pro Pro Ala Ile Tyr 130 Lys Ser Ser Cys Ser Ile Asp Val Thr Phe 140 Phe Pro Phe  
 360  
 GAC CAG CAG AAC TGC AAG ATG AAG TTT GGC TCC TGG ACA TAT GAC AAG GCC AAG ATC GAT CTG GAG CAG ATG GAG AGG ACA GTG GAC CTG  
 Asp Gln Gln Asn Cys Lys Met 150 Phe Gly Ser Trp Thr Tyr Asp Lys Ala 160 Lys Ile Asp Leu Glu Gln Met Glu Arg Thr 170 Val Asp Leu  
 450  
 AAG GAC TAC TGG GAG AGT GGC GAG TGG GGC ATT ATC AAT GCC ACC GGA ACC TAT TAT Tyr Asn Ser Lys Lys Tyr Asp Cys Cys Ala 200 GAG ATC TAC  
 Lys Asp Tyr Trp Glu Ser Gly 180 Trp Ala Ile Ile Asn Ala Thr Gly Thr 190 Tyr Asn Ser Lys Lys Tyr Asp Cys Cys Ala 200 GAG ATC TAC  
 540  
 CCC GAT GTC ACC TAC TTT GTG ATC CGC CGG CTG CCG CTG TTC TAT ACC ATC ATC ATC CCA TGC CTG CTC ATC TCC TGC CTC  
 Pro Asp Val Thr Tyr Phe 210 Ile Arg Arg Leu Pro Leu Phe Tyr Thr 220 Ile Asn Leu Ile Ile Pro Cys Leu Leu Ile Ser Cys Leu 230  
 630  
 ACT GTG CTC GTG TTC TAC CTG CCT TCC GAG TGT GGA GAG AAG ATC ACG CTG TGC TGC CTG CTG CTA TCT CTC ACT CTC CTC CTC CTC  
 Thr Val Val Leu Val Phe Tyr Leu 240 Ser Glu Cys Gly Glu Lys Ile Thr Leu 250 Cys Ile Ser Val Leu Leu Ser Leu Thr Val 260 Phe Leu Leu  
 720  
 CTC ATC ACG GAG ATC ATC CCG TCC ACC TCG CTG GTC ATC CCA CTC ATC GGC GAG TAC CTG CTC TTC ACC ATG ATC TTT GTC ACC CTC TCT  
 Leu Ile Thr Glu Ile Ile Pro 270 Thr Ser Leu Val Ile Pro Leu Ile Gly 280 Glu Tyr Leu Leu Phe Thr Met Ile Phe Val 290 Thr Leu Ser  
 810

FIG.15C-2



ATC GTT ATC ACA GTC TTC GTG CTC 900 AAT GTA CAC CAC CGC ICC CCC AGC ACC CAC AAC ATG CCC AAC TGG GTA AGG GTA GCC CTG CTA GGC  
11e Val 11e Thr Val Phe Val 300 Leu Asn Val His His Arg Ser Pro Ser Thr His Asn Met Pro Asn Trp Val Arg Val Ala Leu Leu Gly  
CGG GTG CCC AGG TGG CTG ATG ATG AAC CGG CCC CTG CCA CCT ATG GAG CTC CAT GGC TCC CCG GAT CTG AAG CTC AGC CCC TCA TAC CAT  
Arg Val Pro Arg Trp Leu Met 330 Met Asn Arg Pro Leu Pro Pro Met Glu Leu His Gly Ser Pro Asp Leu Lys Leu Ser Pro Ser Tyr His  
TGG CTA GAG ACT AAC ATG GAT GCT 1080 GGA GAA AGG GAG GAG ACA GAG GAA GAG GAA GAA GAT GAA AAC ATA TGT GTG TGT GCA GGC  
Trp Leu Glu Thr Asn Met Asp 360 Gly Glu Arg Glu Glu Thr Glu Glu Glu Glu Glu Asp Glu Asn Ile Cys Val Cys Ala Gly  
CTT CCA GAC TCT TCG ATG GGT GTC 1170 CTC TAT GGC CAT GGC GGC CTG CAT CTG AGA GCC ATG GAG CCT GAG ACC AAG ACT CCA TCC CAG GCT  
Leu Pro Asp Ser Ser Met Gly Val 390 Leu Tyr Gly His Gly Gly Leu His Leu Arg Ala Met Glu Pro Glu Thr Lys Thr Pro Ser Gln Ala  
AGC GAG ATT CTG CTG TCA CCT CAA 1260 ATA CAG AAA GCA CTA GAA GGT GTA CAC TAC ATT GCT GAC CGT CTG AGG TCT GAG GAT GCT GAC TCT  
Ser Glu Ile Leu Leu Ser Pro Gln 420 Ile Gln Lys Ala Leu Glu Gly Tyr Val His Tyr Ile Ala Asp Arg Leu Arg Ser Glu Asp Ala Asp Ser  
TCG gtgagt.....ctaacttcag 1350 GTG AAG GAA GAC TGG AAG TAT GTG GCC ATG GTG GTA GAC CGG ATA TTC CTC TGG CTG TTC ATT ATC  
Ser Val Lys Glu Asp Trp Lys 450 Val Lys Glu Asp Trp Lys Tyr Val Val Ala Met Val Val Asp Arg Ile Phe Leu Trp Leu Phe Ile Ile  
GTC TCG TTC CTG GGG ACC ATC GGA CTC TTC CTT CCT CCA TTC CTG GCT GGA ATG ATC TAA CTTCATGTCCTTCATGTTGGCTCCCAAGGTGGCCTTCGTA  
Val Cys Phe Leu Gly Thr Ile Gly Leu Phe Leu Pro Pro Phe Leu Ala Gly Met Ile 480  
1500 ACTATCTTCTAGTCTCTGTGAATGGAGCCATCTCTAGANTACTCTTTTGAC.....3'  
1530  
1410  
1440  
1380  
1470

FIG.15C-3

[illegible]

### SIGNAL PEPTIDE

[illegible][illegible]

### MEMBRANE SPANNING III

ALPHA1  
IDTQWVHFFSTKWRPSROKQEKRIFTEDIDISDICKGPPPPGDFH  
ALPHA2  
LGVADRWLWNNRRLPPMELHGPSOLKLSPSYHWLEINMDAGERETEETEEEEEEDENICVACAGLPDSSMGVLYGHGGHLHRAWEPETKTPSOA  
ALPHA3  
LNLQVRVFMVTRTSGEDTPTKTRTFYGAELSNLNGFSRADSKSKGEGYPCQDGTGCGYCHHRAVKISNE SANLTRSSSESSESVHAYL  
ALPHA4  
LDIVRLLFLFKWRPSVVDXNCARLIESNHKKMANAPRSEWPEGVGEGLISDIGNOGLSPARTFCNPTDTAVEYTOPICRSPPLEVDPOLKTSEVEKASPCPSPGSCPPPKSSSGAPHLIKA  
CYTOSOLASMIC REGION

## CYTOPLASMIC REGION

ALPHA1  
ALPHA2  
ALPHA3  
ALPHA4

SPLIKHTEVKSSTEGKXETUKSD  
SEILLSPQIQKALEGPHIADRLRSE  
SLSALSSEIKETOSTXENHWKAO  
KSLSVQHVPPSSQEAEDGIRCSRSRISQYCVSGDGAASLADSKPTSSPTSLKARPSOLPVDSDQASPCCKCTCKEPPVSPVPTVLKAGGTAKAPQHLPLPSL  
RSLSVQHVPPSSQEAEDGIRCSRSRISQYCVSGDGAASLADSKPTSSPTSLKARPSOLPVDSDQASPCCKCTCKEPPVSPVPTVLKAGGTAKAPQHLPLPSL

AMPHIPATHIC HELIX  
CYTOPLASMIC REGION

## CYTOPLASMIC REGION

ALPHA1 QESNAAAEKFKRQVQVHMLGVYVJLQVILAVDAGRLIELHQOQ  
 ALPHA2 DADSSVKEDKRLQVQVHMLVILGFLVIGLELPPFLAGLI  
 ALPHA3 NVAKEIQDDKRLQVQVHMLGVYVJLQVILAVDAGRLQLOPLMARDDT  
 ALPHA4 OTDFSVKEDKRLQVQVHMLGVYVJLQVILAVDAGRLQLOPLWLAGLI

## MEMBRANE SPANNING IV

Fig. 16



FIG.17A

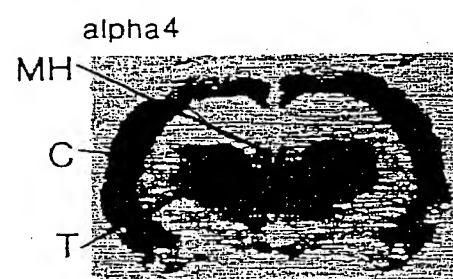
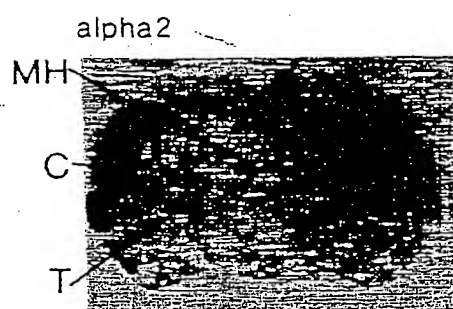
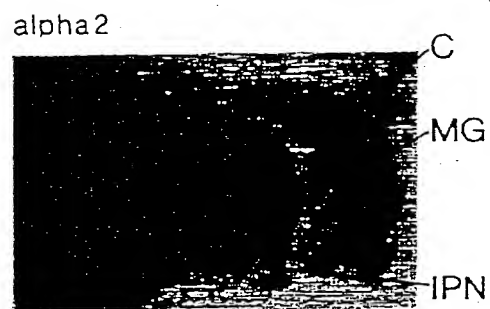


FIG.17B



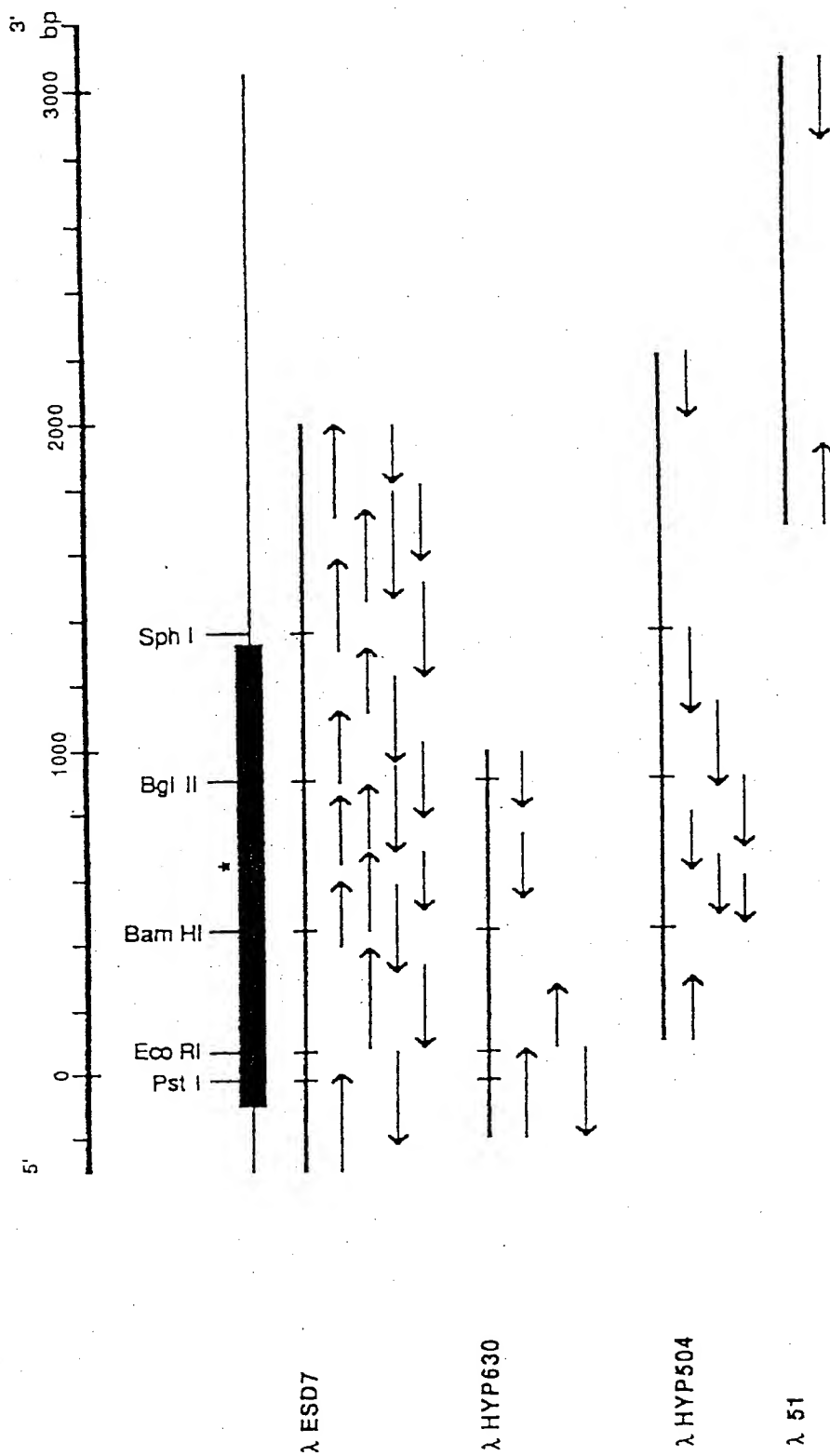


FIG.18A

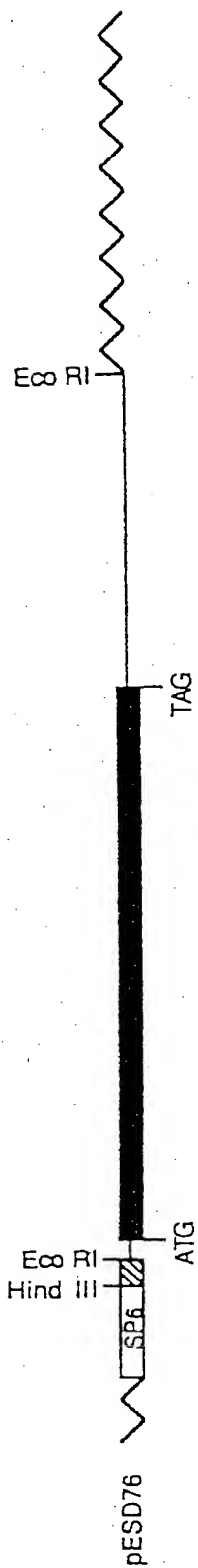
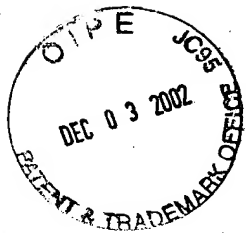


FIG.18B





150  
Gln Asn Cys Ser Met Lys Phe Gly Ser Trp Thr Tyr Asp Gly Thr Met Val Asp Leu Ile Leu Ile Asn Glu Asn Val Asp Arg Lys Asp  
CAG AAC TGC TCG ATG AAG TTT GGA TCC TGG ACT TAC GAC GGT ACC ATG GTT GAC CTC ATT CTA ATC AAT GAA AAC GTT GAC CGG AAA GAC  
440 460 500  
170  
Phe Phe Asp Asn Gly Glu Trp Glu Ile Leu Asn Ala Lys Gly Met Lys Gly Asn Arg Arg Glu Gly Phe Tyr Ser Tyr Pro Phe Val Thr  
TTT TTT GAT AAC GGA GAG TGG GAG ATA CTC AAC GCA AAG GGG ATG AAG GGC AAC AGA AGA GNA GGC TTT TAC TCC TAT CCG TTT GTT ACC  
520 540 560 580 600  
180  
Tyr Ser Phe Val Leu Arg Arg Leu Pro Leu Phe Tyr Thr Leu Phe Leu Ile Ile Pro Cys Leu Gly Leu Ser Phe Leu Thr Val Leu Val  
TAC TCT TTT GTC CTG AGA CGC CTG CCC TTG TTT TAC ACG CTC TTT TTG ATA ATC CCC TGC CTG GGG TTG TCT TTT CTC ACG GTC CTG GTG  
620 640 660 680  
210  
Phe Tyr Leu Pro Ser Asp Glu Gly Glu Lys Leu Ser Leu Ser Thr Ser Val Leu Val Ser Leu Thr Val Phe Leu Val Ile Glu Glu  
TTC TAC CTA CCC TCG GAC GAA GGG GAA AAA CTC TCA TTA TCC ACC TCC GGT TTG GTC TCT TTG ACG GTG TTT CTT TTA GTG ATT GAA GAA  
700 720 740 760 780  
240  
Ile Ile Pro Ser Ser Lys Val Ile Pro Leu Ile Gly Glu Tyr Leu Leu Phe Ile Met Ile Phe Val Thr Leu Ser Ile Ile Val Thr  
ATA ATC CCG TCC TCT TCG AAG GTC ATC CCC CTC ATT GGC GAG TAC CTC CTC TTC ATT ATG ATT TTT GTC ACG CTG TCT ATT ATC GTC ACG  
800 820 840 860  
270  
Val Phe Val Ile Asn Val His His Arg Ser Ser Ser Thr Tyr His Pro Met Ala Pro Trp Val Lys Arg Leu Phe Leu Gln Arg Leu Pro  
GTT TTT GTA ATT AAT GTC CAC CAC CAC AGA TCT TCC TCA ACG TAC CAT CCC ATG GCC CCC TGG GTG AAG AGG CTG TTT CTA CAA AGA CTC CCG  
880 900 920 940 960  
300  
Arg Trp Leu Cys Met Lys Asp Pro Met Asp Arg Phe Ser Phe Pro Asp Gly Lys Glu Ser Asp Thr Ala Val Arg Gly Lys Val Ser Gly  
AGA TGG CTT TGC ATG AAG GAC CCC ATG GAC CGC TTC TCT TTC CCG GAT GGA AAG GAG AGT GAT ACA GCC GTG AGG GGG AAA GTC TCA GGC  
980 1000 1020 1040

FIG.19B



360 370 380  
Lys Arg Lys Gln Thr Pro Ala Ser Asp Gly Glu Arg Val Leu Val Ala Phe Leu Glu Lys Ala Ser Glu Ser Ile Arg Tyr Ile Ser Arg  
AAA AGG AAA CAG ACT CCC GCC AGC GAT GGA GAA AGA GTT CTG CTC GCT TTC CTC GAG AAG GCC TCC GAG TCC ATC AGA TAC ATT TCG AGG  
1060 1080 1100 1120 1140  
390 400 410  
His Val Lys Lys Glu His Phe Ile Ser Glu Val Val Gln Asp Trp Lys Phe Val Ala Gln Val Leu Asp Arg Ile Phe Leu Trp Leu Phe  
CAT GTG AAA AAG GAA CAC TTC ATC ACC CAG GTA GTG CAA GAC TGG AAA TTT GTG GCT CAA GTT CTG GAC CGC ATC TTC CTG TGG CTC TTT  
1160 1180 1200 1220  
420 430  
Leu Ile Ala Ser Val Leu Gly Ser Ile Phe Ile Pro Ala Leu Lys Met Trp Ile His Arg Phe His  
CTG ATA GCT TCT GTG TTG GGT TCC ATT CTG ATT TTT ATT CCA GCC TTG AAG ATG TGG ATA CAT CGT TTC CAC TAG GAGCCACTCTCTGGACCCA  
1240 1260 1280 1300 1320  
TTTGAAGACATACATAGACACAATCCCACTTAGGACTGACAGCGGCTGSCATGCTGACAGGAAGCAGAGCCATCGTAGTGGTGCCCTTGTCTCTGGGAGCTTTCTGTG  
1340 1360 1380 1400 1420 1440  
ATTGAGGGCACTGACAGAAATGTGGGTTTGAGTTAGTGACATGGTGGCTGCCATTAGAGGTGTAGTTGGGCAATTTGGAGAGCTCTCCATGTTATATTGTTATGTGGGAGTTCTCTGAAC  
1460 1480 1500 1520 1540 1560  
TACTCCCTCTGCTCATCCCTGAAGCCACTGGGGCTATGTGGTATTTCTTAGCAGTGTGCTGTAAGCCCAATTTTGACAATAGTTTTCAGGAATTCAGGAGTACAACTCTCCACACACAGG  
1580 1600 1620 1640 1660 1680  
TCAAATTTGCCACTTGTCAACGAGTGTCCACAAATAGGGTCATTTGAAGATGACCTTGAATGGCTATGACAGTTCCTCTAAGCCAGGTGTTACTGGAACTTTCCTCAGCTGACCTGGGAC  
1700 1720 1740 1760 1780 1800  
TTTTCGAATGCCAGTAGGAACCTCGGGTGATTTCTAGCTTTCCTGTAGGTTCCATCAAAATTAACCTTACCCCAAGAAACAGCCCAATTCGCTAGTAGAACTGTATTTATTCACACACATCTC  
1820 1840 1860 1880 1900  
TTTTTTTCCC.....3'  
1930

FIG.19C



NEURONAL NICOTINIC ACETYLCHOLINE RECEPTOR SUBUNITS

BETA 3	MTGFLRFLVLSATLSGSSWTLTATAGLSSVAFHEDALLRHLFOGOKKVPVVLNLSGDIKVVYFGLKISQIVQVQKNEIMTNVAKDEMTDOKLRWANEYEGGI
BETA 2	MLACUAGHSNVALFESLLWLCSGVLGTDIGERLVEHLDPSSYKLIIPATNGSELVTVOLMVSALGSIHQRECIQITIAVMTDEEYRITWKREDFDNM
ALPHA 2	MTLSHSALOFWTHLYWCLLLVPAVLLTOOGSHTHADRLFKH LFGDQARWADVPVNTSOWIVFGLSIALIDQIKAPATITIAVAKDEEYRITWKREDFDNM
ALPHA 3	MGVLLPPPLSLMLVLVLLPAAASAAGHRLFOY LFGDQARWADVPVNTSOWIVFGLSIALIDQIKAPATITIAVAKDEEYRITWKREDFDNM
ALPHA 4	MEIGGPGAPPPPLLLPLLLLTGTLGPASSHIETRAHAEERLLKR LFGDQARWADVPVNTSOWIVFGLSIALIDQIKAPATITIAVAKDEEYRITWKREDFDNM
	<-----SIGNAL PEPTIDE----->
BETA 3	NSIKVQSESLQDDIVTFENADRRFEGSLTKAIVKSSGTVSMIPPAKYKSSGTVMTFEPTDRONGSWKIGSWTIDGTAVQILILINEMVORKDFDNRWEILNAKG
BETA 2	KKVRLQSKHMLDDVLYNIADGAYEVSYFYSNMAVSYDGSIFMLPPAIKYKSAKIEKHFPTDQNDCTWKIRGWTIDGATEIDVLKSDVASLDDTPSRWQIILALPG
ALPHA 2	TSLRVQSEMIWIPDILVLYNADGFAVTHMTKALHFFTGTVHWPPAIKYKSSGIDYTFPTDQNDCTWKIRGWTIDGATEIDVLKSDVASLDDTPSRWQIILALPG
ALPHA 3	EFARVLAEEKIKKDDILVLYNADGFAVTHMTKALHFFTGTVHWPPAIKYKSAKIEKHFPTDQNDCTWKIRGWTIDGATEIDVLKSDVASLDDTPSRWQIILALPG
ALPHA 4	TSIRIQSELWRRPDILVLYNADGFAVTHMTKALHFFTGTVHWPPAIKYKSSGIDYTFPTDQNDCTWKIRGWTIDGATEIDVLKSDVASLDDTPSRWQIILALPG
	<-----TMD 1----->
BETA 3	WKGNNR EGFYS IPFVTSFVLRRLDIFYLFLIIPCGLSEITVVFYLPDSDEGKLSLTSVLVSLTIVLLVFEIINSSKVLITICETILITIMIFVILSIV
BETA 2	RRNENPDOSTTVDIIVDFIIRKRLFYIINLIIPCGLITSAIIVFYLPDSDEGKLSLTSVLVSLTIVLLVFEIINSSKVLITICETILITIMIFVILSIV
ALPHA 2	TYNSKKYDCCAEIIPDVITVFVIRRLDIFYLFLIIPCGLISCTIVVFYLPDSDEGKLSLTSVLVSLTIVLLVFEIINSSKVLITICETILITIMIFVILSIV
ALPHA 3	YKHEIKYNCCAEIIPDVITVFVIRRLDIFYLFLIIPCGLISCTIVVFYLPDSDEGKLSLTSVLVSLTIVLLVFEIINSSKVLITICETILITIMIFVILSIV
ALPHA 4	TYNTRKYECCEAIIPDIINAFIIRRLDIFYLFLIIPCGLISCTIVVFYLPDSDEGKLSLTSVLVSLTIVLLVFEIINSSKVLITICETILITIMIFVILSIV
	<-----TMD 1----->
BETA 3	TVFVIRWVHSSSTVMPAPVWKRLFQRLRWLCHKDPMDGFSPDGK
BETA 2	SVQVIRWVHSSSTVMPAPVWKRLFQRLRWLCHKDPMDGFSPDGK
ALPHA 2	TVFVIRWVHSSSTVMPAPVWKRLFQRLRWLCHKDPMDGFSPDGK
ALPHA 3	TVFVIRWVHSSSTVMPAPVWKRLFQRLRWLCHKDPMDGFSPDGK
ALPHA 4	TVFVIRWVHSSSTVMPAPVWKRLFQRLRWLCHKDPMDGFSPDGK
	<-----TMD 1----->
BETA 3	PLEVPDLKTSEVEKASPCSPGSCPPPKSSSGAPMLIKARLSVQHVHPSQEAEDGIRCSRNSIOYCVSODGAASLADSKPTSSPTSLKARPSOLPVSDOASPCKCT
BETA 2	PLEVPDLKTSEVEKASPCSPGSCPPPKSSSGAPMLIKARLSVQHVHPSQEAEDGIRCSRNSIOYCVSODGAASLADSKPTSSPTSLKARPSOLPVSDOASPCKCT
ALPHA 2	PLEVPDLKTSEVEKASPCSPGSCPPPKSSSGAPMLIKARLSVQHVHPSQEAEDGIRCSRNSIOYCVSODGAASLADSKPTSSPTSLKARPSOLPVSDOASPCKCT
ALPHA 3	PLEVPDLKTSEVEKASPCSPGSCPPPKSSSGAPMLIKARLSVQHVHPSQEAEDGIRCSRNSIOYCVSODGAASLADSKPTSSPTSLKARPSOLPVSDOASPCKCT
ALPHA 4	PLEVPDLKTSEVEKASPCSPGSCPPPKSSSGAPMLIKARLSVQHVHPSQEAEDGIRCSRNSIOYCVSODGAASLADSKPTSSPTSLKARPSOLPVSDOASPCKCT
	<-----CYTOPLASMIC REGION----->
BETA 3	ESDTAVRGVSKGRKOTP ASDGERVLVAFLEKASESIRYISRHVKKHEFISOVVQDQKFAZQVDRIFLWALIASVLGSLILIPALKWVHFRFH
BETA 2	ASVOGLAGAFRAEPTAG PGRSVGPCSCGLREAYGVGRFIADHMRSEDDQSVRECHWTAQVQIDRFLNTVFVGVGTGVGULQPLFONATYATTLHPDHSAPSSK
ALPHA 2	YGHGGLHRAEPETKTP SOASEILLSPOIOKALEGVHYIADRLHSEDADSSVKEKWTALVWVIRLWVLIIVCFLEGTIGLEPPFLAGMI
ALPHA 3	ISNFSANLTRSSSESVN AVLSLSALSPEIKELIOSVKYIAENKAKONVAKEIODQKTYANQIDRIFLWVILVLCILGTAGLQPLMARDOT
ALPHA 4	CKEPSVSPVTLKAGGTAKAPPOLPLSPALTRAVEGVQYIADHLKAEADTQSVKEQKTYANQIDRIFLWVLIIVCLLGTIVGLEPPWLAAC
	<-----TMD 1V----->

FIG.20

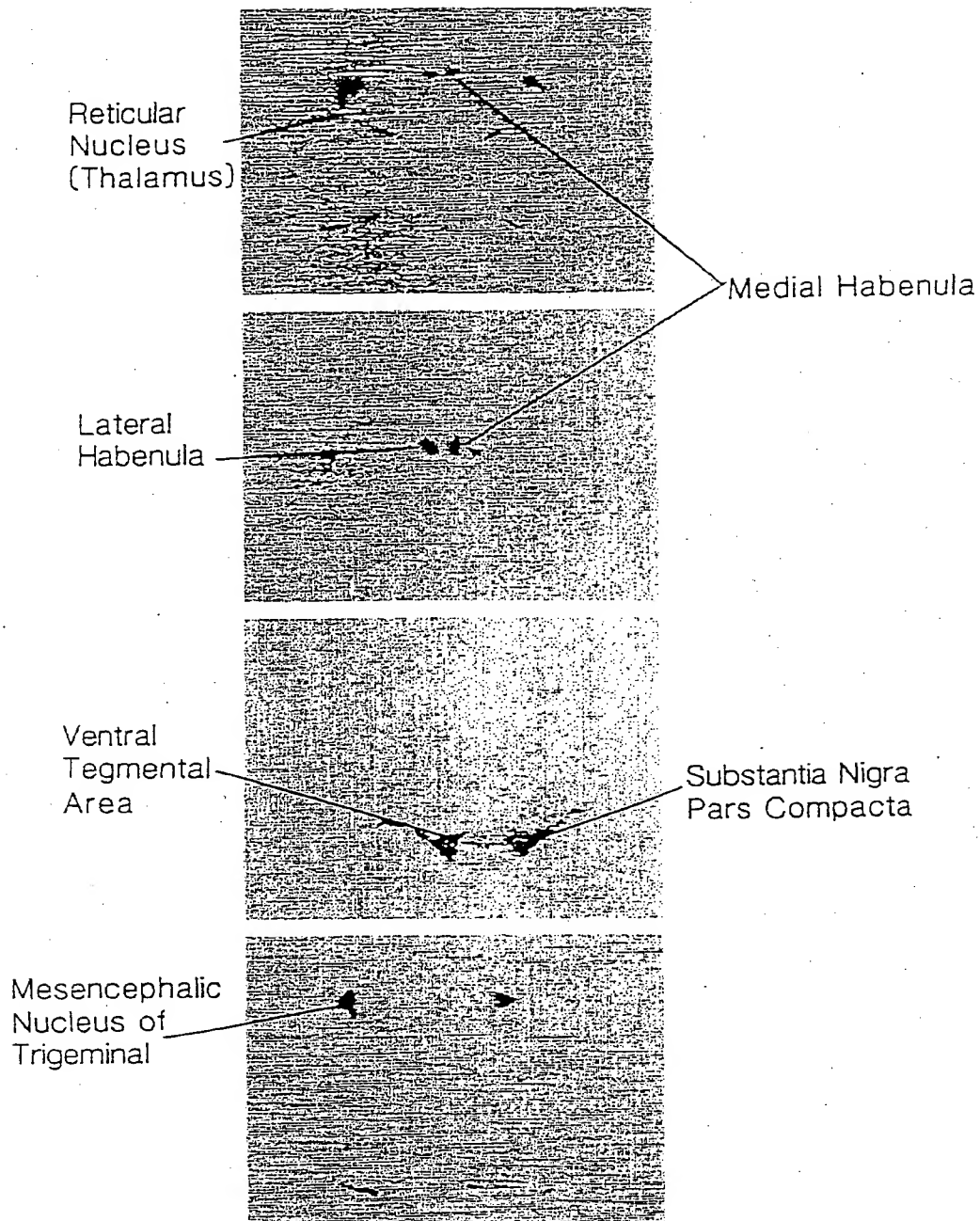


FIG.21

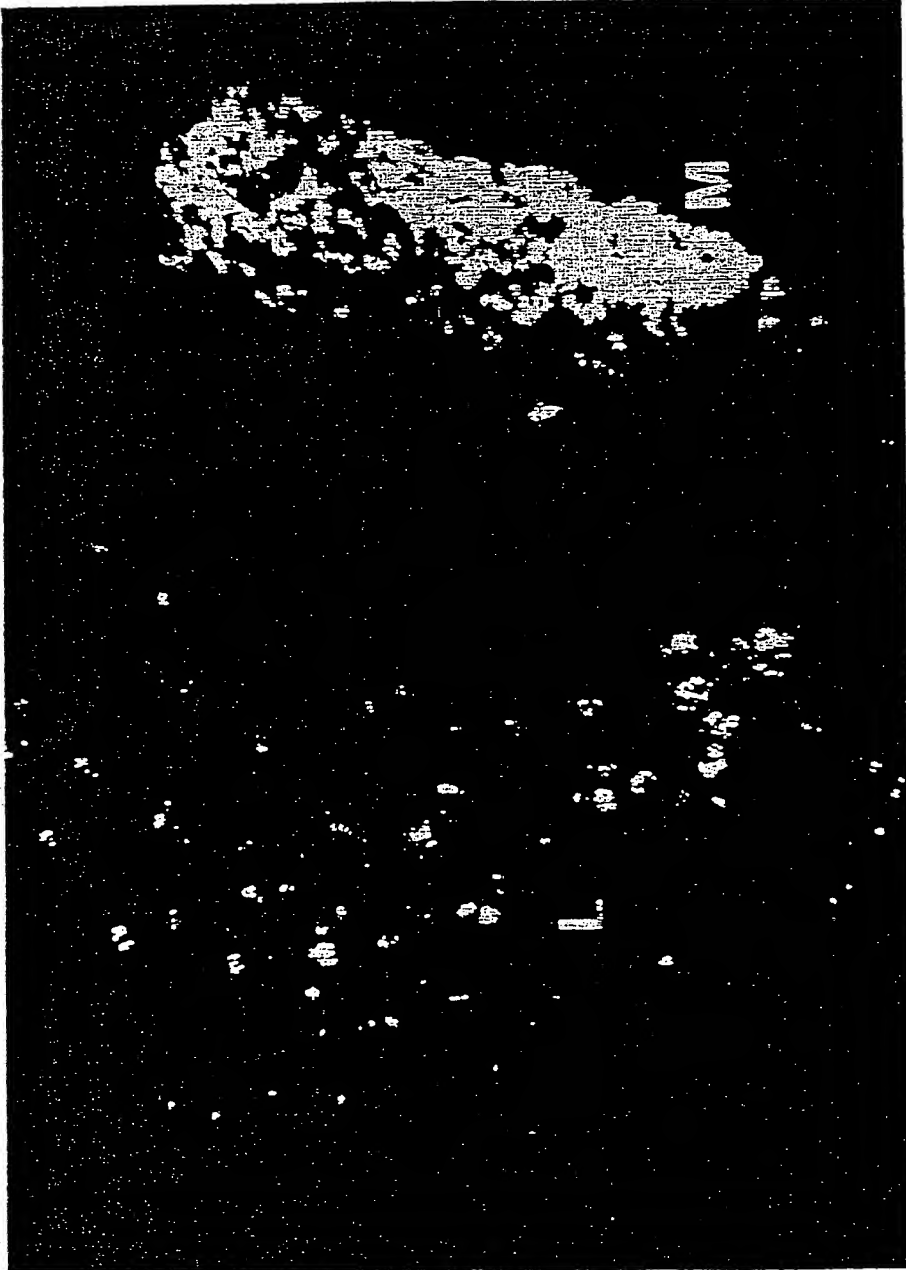


FIG.22

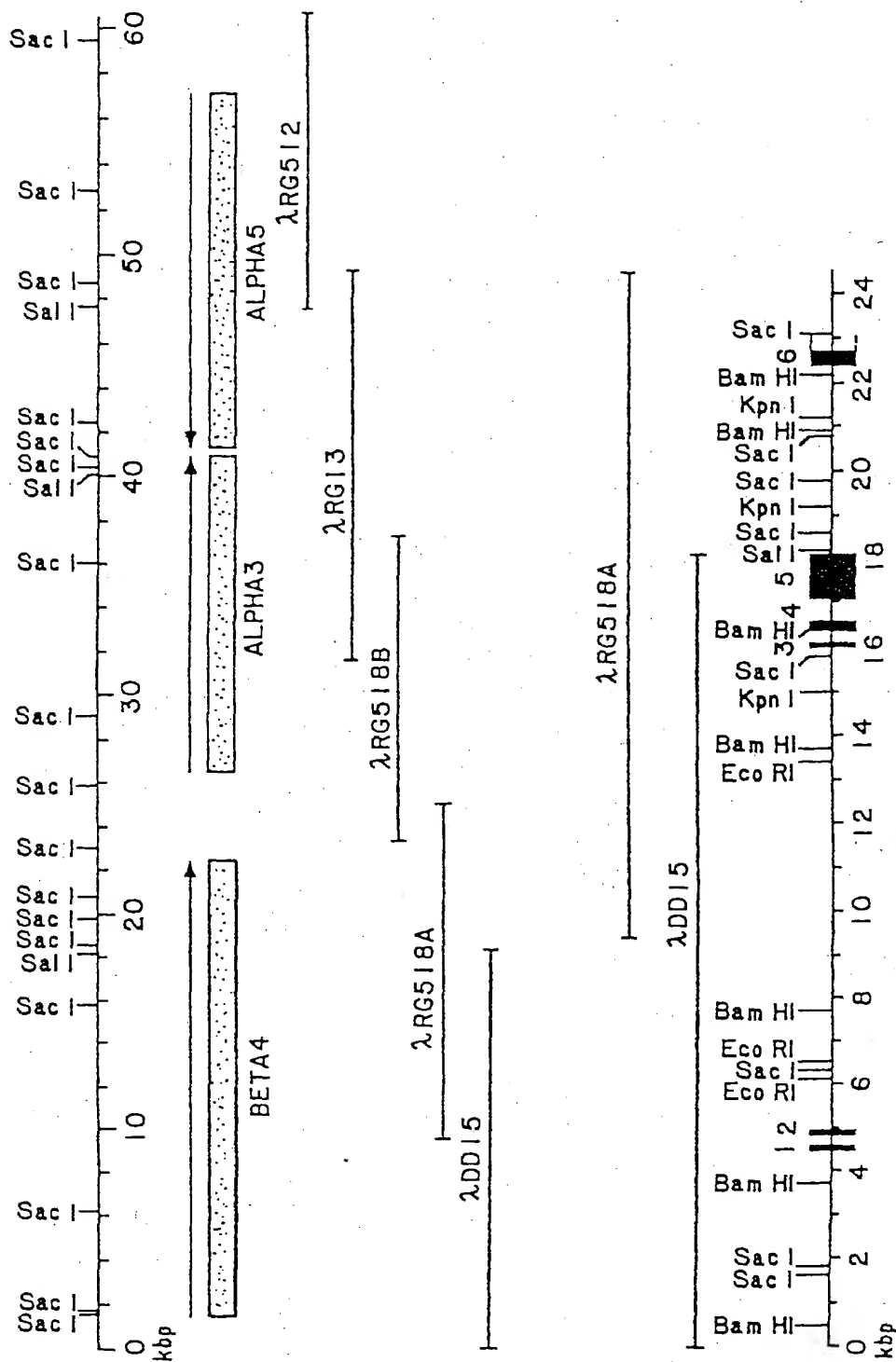


FIG.23





130 Ala Ile Tyr Lys Ser Ala Cys Lys Ile Glu Val Lys His Phe Pro Phe Asp Gln Gln Asn Cys Thr Leu Lys Phe Arg Ser Trp Thr Tyr  
 GCT ATC TAC AAG AGT GCC TGC AAG ATT GAG GTG AAG CAC TTT CCC TTC GAC CAG CAG CAG AAT TTC CGC TCC TGG ACC TAT  
 380 400 420 440 150  
 160 Asp His Thr Glu Ile Asp Met Val Leu Lys Ser Ala Thr Ala Ile Met Asp Asp Phe Thr Pro Ser Gly Glu Trp Asp Ile Val Ala Leu  
 GAC CAC ACG GAG ATT GAC ATG GTT CTT AAG TCG CCC ACG GCC ATC ATG GAT GAC TTC ACC CCC AGT GGT GAA TGG GAC ATT GTG GCC CTC  
 480 500 520 540 180  
 190 Pro Gly Arg Arg Thr Val Asn Pro Gln Asp Pro Ser Tyr Tyr Val Asp Val Thr Tyr Asp Phe Ile Ile Lys Arg Lys Pro Leu Phe Tyr Thr  
 CCA GGA CGG AGG ACG GTG AAC CCT CAG GAC CCC ACG TAC GTG GAC GTG ACC TAT GAC TTC ATC ATC AAG CGC AAC GCG CTC TTC TAC ACC  
 560 580 600 620 210  
 220 Ile Asn Leu Ile Ile Pro Cys Val Leu Ile Thr Ser Leu Ala Ile Leu Val Phe Tyr Leu Pro Ser Asp Cys Gly Glu Lys Met Thr Leu  
 ATC AAT CTT ATC ATT CCT IGT GTG CTC ATC ACC TCG CTG GCT ATC CTG GTC TTC TAC CTG CCC TCC GAC TGT GGG GAG AAG ATG ACG CTC  
 660 680 700 720 240  
 250 Cys Ile Ser Val Leu Leu Ala Leu Thr Phe Phe Leu Leu Leu Ile Ser Lys Ile Val Pro Pro Thr Ser Leu Asp Ile Pro Leu Ile Gly  
 TGC ATC TCT GTG CTG CTG GCA CTC ACG TTC TTC CTG CTG CTC ATC TCC AAG ATC GTG CCT CCC ACC TCC CTT GAC ATA CCG CTC ATT GGC  
 740 760 780 800 270  
 280 Lys Tyr Leu Leu Phe Thr Met Val Leu Val Thr Phe Ser Ile Val Thr Thr Val Cys Val Leu Asn Val His His Arg Ser Pro Ser Thr  
 AAG TAC CTC TTG TTC ACC ATG GTG CTG GTC ACC TTT TCC ATC GTC ACC ACT GTG TGT GTC CTC AAT GTG CAC CAC GCG TCA CCC AGC ACT  
 840 860 880 900 300  
 310 His Thr Met Ala Ser Trp Val Lys Glu Cys Phe Leu His Lys Leu Pro Thr Phe Leu Phe Met Lys Arg Pro Gly Leu Glu Val Ser Leu  
 CAC ACC ATG GCA TCC TGG GTC AAG GAG TGC TTC CTG CAC AAA CTG CCC ACC TTC CTC TTC ATG AAG CGT CCC GGT CTT GAA GTC AGC CTG  
 920 940 960 980 330

FIG.24B





340 Val Arg Val Pro His Pro Ser Gln Leu His Leu Ala Thr Ala Asp Thr Ala Ala Thr Ser Ala Leu Gly Pro Thr Ser Pro Ser Asn Leu  
350 360  
3TC AGG GTC CCT CAT CCC AGC CAG CTG CAC TTT GTG AAC CCT GTC CCT GCT GCC ACA GCT GAT ACT GCA GCC ACC TCT GCC TTA GGC CCC ACC AGC CCA TCC AAC CTC  
1020 1040 1060 1080

370 Tyr Gly Ser Ser Met Tyr Phe Val Asn Pro Val Pro Ala Ala Pro Lys Ser Ala Val Ser Ser His Thr Ala Gly Leu Pro Arg Asp Ala  
380 390  
TAT GGG AGT TCC ATG TAC TTT GTG AAC CCT GTC CCT GCT GCC GCT CCT AAG TCT GCA GTC AGC TCC CAC ACA GCA GGC CTC CCC AGG GAT GCC  
1100 1120 1140 1160

400 Arg Leu Arg Ser Ser Gly Arg Phe Arg Glu Asp Leu Gln Glu Ala Leu Glu Gly Val Ser Phe Ile Ala Gln His Leu Glu Ser Asp Asp  
410 420  
CGT CTG AGG TCC TCC GGG AGG TTC CGG GAA GAT CTA CAG GAA GCA TTA GAG GGT GTC AGC TTC ATC GCC CAG CAT CTG GAG AGC GAT GAC  
1200 1220 1240 1260

430 Arg Asp Gln Ser Val Ile Glu Asp Trp Lys Phe Val Ala Met Val Val Asp Arg Leu Phe Leu Trp  
440  
CGA GAT CAA AGT gtagtcaactg... ...ttgtctgcag GTC ATC GAG GAC TGG AAG TTC GTC GCG ATG GTT GTT GAC CGC CTC TTC CTG TGG  
1280 1300 1320 1340

450 Val Phe Val Phe Val Cys Ile Leu Gly Thr Met Gly Leu Phe Leu Pro Pro Lys Asp Ser  
460 470  
GTG TTC GTG TTT GTG TGT ATT CTG GGC ACC ATG GGG CTC TTC CTG CCA CCC CTT TTC CAG ATC CAC GCA CCC TCC AAG GAC TCC TAG GCT  
1340 1360 1380 1400 1420

ACCCGCGNTGTCCTCGGNNCCGGGAAGTAGTGAGATGATATAGAACGCGGTGGGAAGCAGGCGGTGTCTTNGGGCTACCCGGGCTGTCTCTCGGGCCCCGGGAAGTAGTGACATGATATGA  
1420 1440 1460 1480 1500 1520

GAAAGCGGTGGGAAGCAGGCGGTGTCTTCGG...3'  
1540

FIG.24C



CGTTGCTGGCCCTCGGGGTCGGAGTTATCCGGAGGGCCGTCGGGGGCGATGGCGGTGCGGGGCTGCGGCTGCTCTTG  
-180 -160 -140 -120 -100  
Met Val Gln Leu Leu Ala Gly Arg Trp Arg Pro Thr Gly Ala Arg Arg Gly Thr Ala Gly Gly Leu Pro Glu Leu Ser Ser Ala Ala Lys  
ATG GTG CAG CTG CTG GCA GGG CGG TGG CGG ACC CGG GCG GCG CGG GGC GGC ACG CGG GGA GGG TTG CCT GAA CTA TCC TCT GCT GCC AAA  
-80 -60 -40  
His Glu Asp Ser Leu Phe Arg Asp Leu Phe Glu Asp Tyr Glu Arg Trp Val Arg Pro Val Glu His Leu Ser Asp Lys Ile Lys  
CAT GAA GAC AGC TTG TTT AGG GAT TTA TTT GAA GAC TAC GAA AGG TGG GTT CGC CCT GTG GAA CAC CTG AGC GAC AAG ATA AAA ATC AAG  
10 20 30 40 50 60 70 80 90  
Phe Gly Leu Ala Ile Ser Gln Leu Val Asp Val Asp Glu Lys Asn Gln Leu Met Thr Thr Asn Val Trp Leu Lys Gln Glu Trp Ile Val Asp  
TTT GGC CTT GCG ATA TCT CAG TTA GTG GAT GTG GAT GAG AAA AAC CAG CTG ATG ACG ACG AAC GTC TGG TTG AAG CAG GAA TGG ATA GAT  
100 120 140 160 180  
Val Lys Leu Arg Trp Asn Pro Asp Asp Tyr Gly Gly Ile Lys Ile Arg Val Pro Ser Asp Ser Leu Trp Ile Pro Asp Ile Val Leu  
GTG AAA TTG AGA TGG AAT CCT GAC GAT TAT GGT GGG ATA AAG ATT ATA CGT GTT CCT TCG GAC TCC CTG TGG ATC CCA GAC ATC GTT TTG  
200 220 240 260 280  
Phe Asp Asn Ala Asp Gly Arg Phe Glu Gly Ala Ser Thr Lys Thr Val Val Arg Val Tyr Asn Gly Thr Val Thr Trp Thr Gln Pro Ala Asn  
TTC GAT AAT GCA GAT GGA CGT TTT GAA GGG GCC AGC ACG AAA ACA GAT GTC GTC AGG TAC AAC GGC ACT GTC ACG TGG ACG CAA CCA GCA AAC  
300 320 340 360 380  
Tyr Lys Ser Ser Cys Thr Ile Asp Thr Phe Phe Pro Phe Asp Leu Gln Asn Cys Ser Met Lys Phe Gly Ser Trp Thr Tyr Asp Gly  
TAC AAA AGT TCT TGC ACC ATC GAC GTT ACC TTT TTC CCG TTT GAT CTC CAA AAT TGT TCC ATG AAA TTC GGC TCG TGG ACA TAC GAT GGA  
400 420 440 460 480  
Ser Gln Val Asp Ile Ile Leu Glu Asp Gln Asp Val Asp Arg Thr Asp Phe Phe Asn Gly Glu Trp Glu Ile Met Ser Ala Met Gly  
TCC CAG GTT GAT ATA ATC CTA GAG GAC CAA GAT GTC GAC AGA ACA GAC TTT TTC GAC AAT GGA GAG TGG GAA ATC ATG AGC GCG ATG GGG  
500 520 540 560 580  
Ser Lys Gly Asn Arg Thr Asp Ser Cys Cys Trp Tyr Pro Tyr Ile Thr Tyr Ser Phe Val Ile Lys Arg Leu Pro Leu Phe Tyr Thr Leu  
AGC AAG GGG AAC CCG ACG GAC AGC TGC TGC TGC TAC CCC TAC ATC ATC ATC TAC TCC TTT GTG ATT AAG CCG CTG CCT CTC TTC TAT ACC TTG  
600 620

FIG.25A

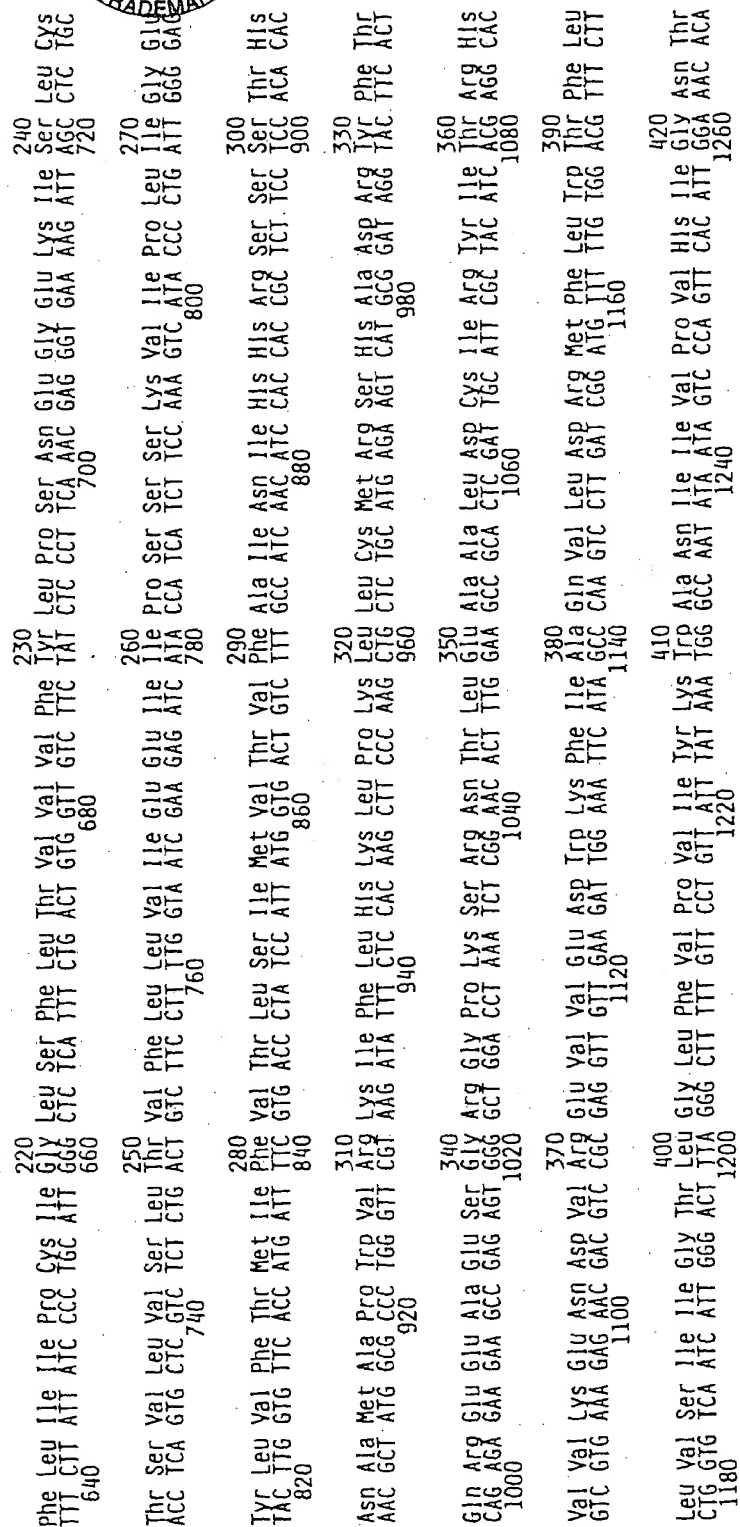


FIG. 25B



lle Lys .  
ATT AAG TGA AACCAAGAAATTACCTGTGGATTAGTAGGAGAGTATGACATGTTATGGAATGTGAAGGTAGTTACAAATTTGACATAGGCTATACA  
1280 1300 1320 1340 1360 1380  
GATTAGCAATTTCTAACATTGGCTTAATGTTGTCCATTAGAACTGCAGTAATAACCTCAAAATAGCAACAACACACATTGTCTGCTGCACTAGTGAAGGCTAGCATCTGCATCCCTGGCAA  
1400 1420 1440 1460 1480 1500  
ACCTACCAAATTTGCAACCAATGATGAAGGCCATCCTTGGAGTGTCTGGAAACTCAACTGATTTTGAAGACTATTTTAAACTCCCCCAAAATTTAGTAGGAACATATATATGTGTGTT  
1520 1540 1560 1580 1600 1620  
TTGAATTTTCAGATGGGTCTTTGGTCTTGTTAAATTGTCTGGGCTAGCACAAAACCTCCTGAGTAGCTGGGACCATGGGTGTGCTCCACTTTGGCCCTGTTCTGTATTTCACAGATATA  
1640 1660 1680 1700 1720  
AAATACATCATTTTATAGGAGGTAGGCCCATTAAGTTGGTTTAAATAACTTAATGTCAAGTTAGGTTTAAATTAACCTTAATGTCAAGCTAAATGTTCTATTGCTGTGAAGAGACATC  
1760 1780 1800 1820 1840  
ATGACCATCAACTCTTATAAAGAAACATTTTCATCAGTGTCTGGCTTACAGTTTGTGAGGTTTACAGCTTATATCAGAGTGAAGCATGATAGCATCCAGGTAGACATTAATGCTGGATCC  
1880 1900 1920 1940 1960  
AGGAGTTCTCTACATCTGGATCAGCGCAGGAGAGAGAGAGCCACTGGACCTGGCTTGAGCATCTGAACCTCAAGCCACCTCCAGTGAACACACACTTCCCCCAACAAGGCC  
2000 2020 2040 2060 2080  
ACACCTCTAATAGTGCCACTTGTGTGATCAAGCATTCAGTCTATGGGTCTACGAGAGCCACTTCTCTAATCAACACACACTTAATAGGATGCTATTCTTTACTGACATTTTAAATAAG  
2100 2120 2140 2160 2180 2200  
CGACAAATGGTAACCTAGAAACATCGTAGGCCACCTTTACTCTTTTATGTTAATGTTGGATTGGCTTTTATATTAACTAGTTTACAGGCTATCTGAAACAACTGTAACAGGCAACTCCTG  
2220 2240 2260 2280 2300 2320  
CAGACACATTTCTTGTAAATGACTTTTAAATCCCTGCAGTGGCATGTTCTTGGTAAATGACTTCAGTCTCTGCTCCACACTCTCCGGTTAGTAGAGCCATTTTATGTATCATCGGCTATCCCTG  
2340 2360 2380 2400 2420 2440  
ATTTGAGAGCAACTGTGCAGTTGCACAGGTTCCACCTCAAAATGGGATGCCATGACCTGTCTGGATAATTTCTGTGGAAACCACTTCTGAGCTGGATACGGTGCCTCATACCTGTCA  
2460 2480 2500 2520 2540 2560  
TGTCTACTTTTCAGGAGGAGAGGCGAGGGGAATTGCTGTGAGTTGTTGGTCAGCCTGGGTTACATATGAGACCCTGTCTCAGAAACCAACCAAAACCTTCCCTGTGTGAGTTGATATAAG  
2580 2600 2620 2640 2660 2680  
CACACTGTCTATATCCGAAATTGGGGATCCTCTAGAGTCGACCTCGAGGCATGCAAGCTTGGCGTAATCATGGTTCATAGCTGTTTCCGTGTGGAATTTGTTATCCG  
2700 2720 2740 2760 2780

FIG.25C



BETA2 MLACHAGHSNMAFSLMLCSGVLGTDTEERLVEHLLDPSSYNKLIIRPATNGSELVTQVMVSLAQIISVHEREQIMTTNVMLTQEMEDYRLTWKPEDFDNMK  
BETA3 HTGFLRVFLVLSATLSGSHVTLTATAGLSSVAEHEDALRLHFGQYQKWVRVNLSSDIKXVYGLKISQLVDVDEKXQLMTTNVWLKQEMTDQKLRMNPPEEYGGIN  
BETA4 MRGTPLLVLSFSLQDQDCRLANAEKLMDDLLNKTRYNNLIIRPATSSQLISIRLELSQLISVNEREQIMTTISWLKQEMTDYRLAMNSSCYEGVN  
----- SIGNAL PEPTIDE -----

BETA2 KVLPSKHMTWLPDVVLYNNADGMYEVSFYSNVSYDGSIFWLPPIYKSACKIEVKHFFPDQONCTMKFRSMTYDRTEIDLVLKSDVASLDDFTSPSGEMDIALPG  
BETA3 SIKVPSSESLWLPDIOLVFENADGRFEGSLMTKAIIVKSSGTVSWTPPASYKSSCTMDVTFPPDRQNCMKFGSWTYOGTWVDLILINENVDKDFDNGEWEILNKG  
BETA4 ILRIPAKRWLPDIOLVLYNNADGMYEVSVYTNVIVRSNGSIQWLPPIYKSACKIEVKHFFPDQONCTLKFRSMTYDHTIEDHVLKSATAIMODFTSPSGEMDIALPG

BETA2 RRNENPDOS TYVDITYDFIIRKKPLFYTTINLIIPCVLITSLAILVFLYLPSCGKMTLCISVLLALTIVFLLLSKIVPPTSLDVLVGYLHFTMVLVTFSTVTSV  
BETA3 HKGNRRREGFYSYPFVTSFVLRRPLFYTLFIIPCLGLSFLTVLVFLYLPSCGKLSLSTSVLVSITVFLVIEEIIIPSSKVIPLIGEYLLFLIMIFVTLISIVTV  
BETA4 RRTVNPQDP SYVDVYDFIIRKKPLFYTTINLIIPCVLITSLAILVFLYLPSCGKMTLCISVLLALTIVFLLLSKIVPPTSLDIPLLGXKLLFTMVLVTFSTVTV  
----- MSR I ----- MSR II ----- MSR III -----

BETA2 CVLNVHHRSPST HTMAPHVKVVFLEKLPITLLFLQPPRHRCARQLRLRRRQREGEAVFIREGPAADPCSVGPCSCG  
BETA3 FVINVHHRSSSTYHPAPHVKNRLFLOLPRWLCHKDPHOREFSPDGKESDTAVRCVSGKXKQTPASDGERVLVAFLEK  
BETA4 CVLNVHHRSPST HTMASHVKECFLHKLPTFTFMKRPGLVSLVRPHESQLHLATADTATSALGTPSPSNLYGSSMYFVNVPVPAAPKSAVSSHTAGLPRDARLRS  
-----

BETA2 LREAVDGVRFIADHHRSEDDQSVREDWKYVAMVIDRLELWTFVVCVGTGVMFLOPLFQNYTATTTLHPDHSAPSSK\*  
BETA3 ASESIRYISRHVKKEHFISQVQDQWKFVAQVLDRIFLFLIASVLGSILIFIPALKMHIRFH\*  
BETA4 SGRFREDLOALEGVSFIAQHLESDDRDQSVIEDWKVAMVVDRIFLVWFVFCILGTMGLFPLPLFQIHAPSXDS\*  
----- MSR IV -----

FIG.26



ALPHA2 HTLSHSALQPMTHLYLWCLLLVPAVLTOQSGSHTHAEDRLFKHLFGGYNRWARVPNTSDVVIVAFGLSIAQLIDVDEKKNQMTTNVWLKQEWNDYKLRWDPAE  
ALPHA3 HGVVLLPPPLSMLMLVLMMLPAASASEAHERLFQYLPEDYNEIIRPVANVSHRPVIOFEVSMQSOLVKVDEVNOMEITNLWLKQIMNDYKLRWKPSD  
ALPHA4 HEIGGCPAPPFLLLPLLLGLTGLLPASSHETRAHAEERLLKRLFGSYNKNWRPVGNISDVULVRGLSIAQLIDVDEKKNQMTTNVWLKQEWNDYKLRWDPGD  
ALPHA5 MVQLLAGRWRTGARRGTAGGLPELSSAAKHEDSLFRDLPEYERWVRPVEHLSDKIKINFGLAISQLVDVDEKKNQMTTNVWLKQEWIDVVKLRWNPDD

SIGNAL PEPTIDE

ALPHA2 FGNVTSRVPSEMIWIPDIVLNNADGEFAVTHMTKAHLFTGTVHVVPPIAYKSSCSIDVTFFPDQONCKMKFGSWTYDKAKIDLEQMENTVDLKDYMESGEWA  
ALPHA3 YQGVEMRVPAPAEKIMKPODIVLYNNADGDFQVDDKTALLKRYTGEVTHPPAIYKSSCKIDVTFFPDQONCKMKFGSWTYDKAKIDLVLGSMNLKDYMESGEWA  
ALPHA4 YENVTSIRIPSELIRWPDIVLYNNADGDFAVTHLTKAHLFDVGRVQWTPPAIYKSSCSIDVTFFPDQONCKMKFGSWTYDKAKIDLVLSIRSVDDQLDYMESGEWV  
ALPHA5 YGGIKIIRVPSDSLWIPDIVLFDNADGRFEGAS TKTVVRYNGTVMTPQANYKSSCTIDVTFFPDQONCKMKFGSWTYDGSQVDIILEDQDQVDRDTDFDNGEWE

\*\*

ALPHA2 IINATGYNKSKYDCCAEIYDPVTYFVIRRLPLFYTNLIIPCLLSLCTLVLFVLPSECGEKITLCISVLLSLTVFLLLITEIIPSTSLVPLIGEYLLFTMIF  
ALPHA3 IIKAPGYKHEIKYNCCAEIYQDITYSLYIRRLPLFYTNLIIPCLLSLCTLVLFVLPSECGEKITLCISVLLSLTVFLLLITEIIPSTSLVPLIGEYLLFTMIF  
ALPHA4 IVDVAGTYNTRKYECCEAEIYDITYAFIIRRLPLFYTNLIIPCLLSLCTLVLFVLPSECGEKITLCISVLLSLTVFLLLITEIIPSTSLVPLIGEYLLFTMIF  
ALPHA5 IMSAMGSKGNRTDSCCH YPYITYSFVIKRLPLFYTNLIIPCLLSLCTLVLFVLPSECGEKITLCISVLLSLTVFLLLITEIIPSTSLVPLIGEYLLFTMIF

MSR I MSR II MSR III

ALPHA2 VTLISIVITVFLVNLVHHRSPSTNNMPN WVRVALLGRVPRWLMHNRPLPHELHGSPDLKLSPSYHKLTHMDAGERETEETEEEDENICVCAGLPDSSMGVLYG  
ALPHA3 VTLISIVITVFLVNLVHRYRTPTHTPT WVKAVFLNLPRVMTHTPTKRTFYGAELSNLNCFSRADSKSCKEGYPCQDGTGCGYCHRRVKISNFSANL  
ALPHA4 VTLISIVITVFLVNLVHHRSPHTMPA WVRVFLDIIVPRLLFMKRPVVKDNCRRLLIESMHKMANAPRFPPEVGPGLSDICNOGLSPAPTCNPTDTAVETOP  
ALPHA5 VTLISIMVTVFAININHRSSSTHNAHPVVRKIFLKLKPLKCHRSADRYFTQREAESGAGPKSRNT

ALPHA2 HGGLHLRAMEPEYKTPSQ  
ALPHA3 TRSSSESQNAV  
ALPHA4 TCRSPLEVPDLKTSSEVEKASPCPSGSCPPPKSSGAPMLIKARSLVQHVPSSQEAEDGIRCHRSRSIQICVSDQGAASLADSKPTSSPTSLKARPSQLPVSDQ  
ALPHA5

ALPHA2 SEILLSPQIOKALEGVHYIADRLRSEDADSSVKEDWKYVAMVVDRIFLWFIIVCFLGTGLFLPPFLAGMI\*  
ALPHA3 SLSALSPETKEAIGSVKYIAENMKAOQNAKEIQDDWKYVAMVVDRIFLWFIIVCFLGTGLFLPPFLAGMI\*  
ALPHA4 ASPCKCTCKEPPSPVTVLKAGGTKAPPQHLPLSPALTRAVEGVQYIADHLKAEDTFSVKEDWKYVAMVVDRIFLWFIIVCFLGTGLFLPPFLAGMI\*  
ALPHA5 LEAALDCIRYITRHHVVKENDVREVEDWKFIAQVLDORMFLWTFLLVSIIGTGLGLFVVPVINGPI\*

MSR IV

FIG.27

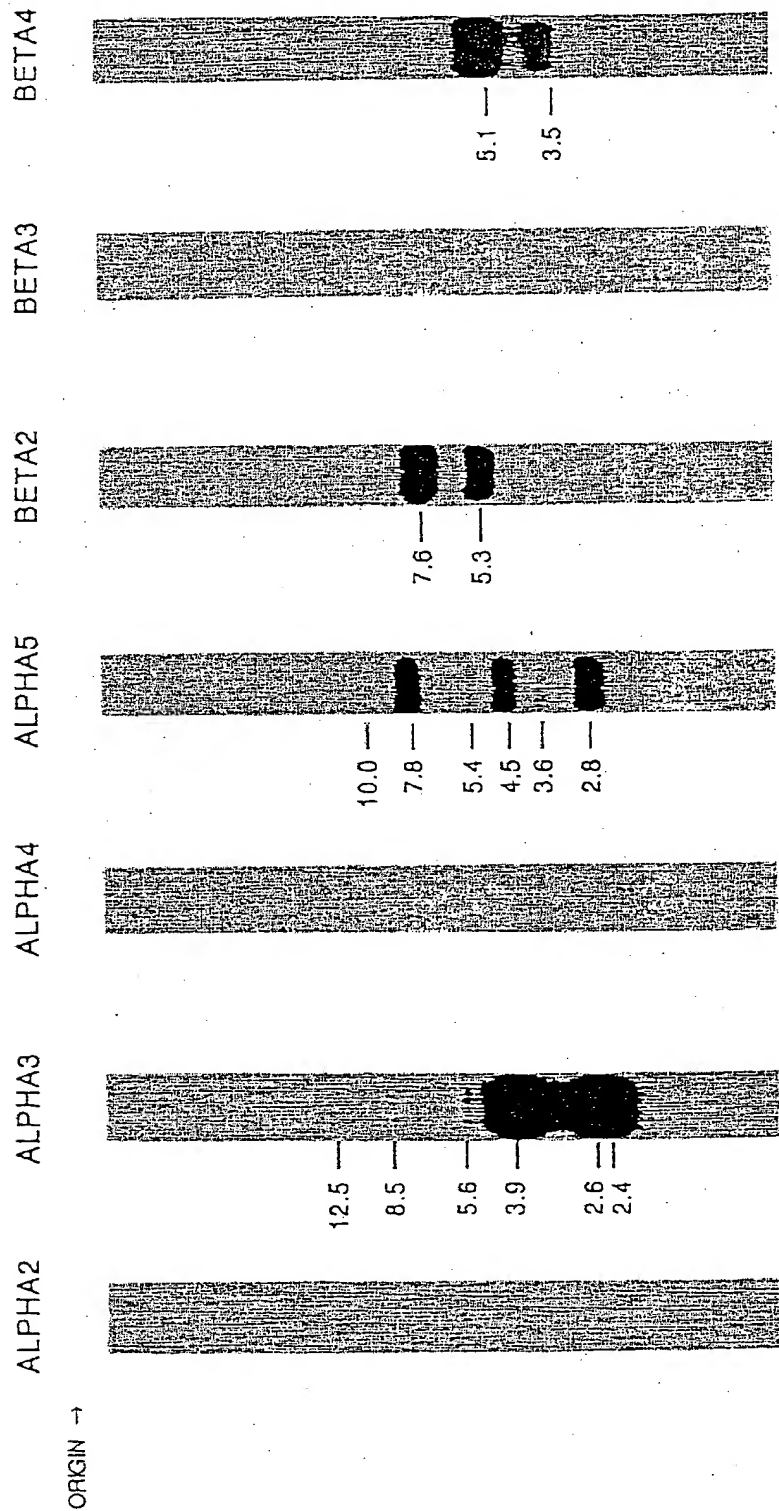


FIG.28



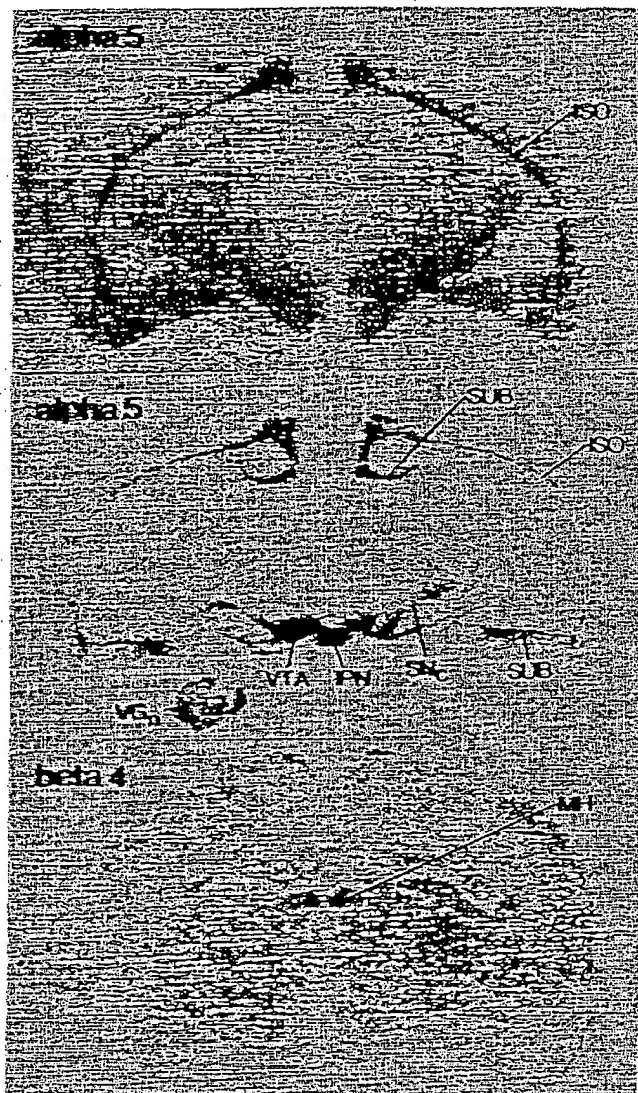
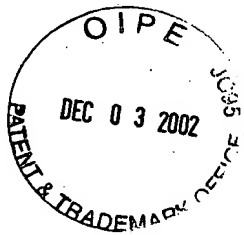


FIG.29